

FIG.1



10 30 50  
 GGC ACC GGG GCG CCG CCG CCG CTG CTG CTA CTG CCG CTG CTG CTG CTC CTA GGG ACC GGC  
 Gly Thr Gly Ala Pro Pro Pro Leu Leu Leu Leu Pro Leu Leu Leu Leu Leu Gly Thr Gly  
 70 90 110  
 CTC TTG CCT GCT AGC AGC CAC ATA GAG ACC CCG GCC CAT GCG GAG GAG CCG CTC CTG AAG  
 Leu Leu Pro Ala Ser Ser His Ile Glu Thr Arg Ala His Ala Glu Glu Arg Leu Leu Lys  
 130 150 170  
 AGA CTC TTC TCC GGT TAC AAC AAG TGG TCT CCG CCA GTA GGC AAT ATC TCA GAT GTG GTC  
 Arg Leu Phe Ser Gly Tyr Asn Lys Trp Ser Arg Pro Val Gly Asn Ile Ser Asp Val Val  
 190 210 230  
 CTC GTC CCG TTT GGC TTG TCC ATT GCT CAG CTC ATT GAC GTG GAC GAG AAG AAC CAG ATG  
 Leu Val Arg Phe Gly Leu Ser Ile Ala Gln Leu Ile Asp Val Asp Glu Lys Asn Gln Met  
 250 270 290  
 ATG ACA ACC AAC GTG TGG GTG AAG CAG GAG TGG CAC GAC TAC AAG CTG CCG TGG GAC CCT  
 Met Thr Thr Asn Val Trp Val Lys Gln Glu Trp His Asp Tyr Lys Leu Arg Trp Asp Pro  
 310 330 350  
 GGT GAC TAC GAG AAT GTC ACC TCC ATC CCG ATC CCC TCT GAA CTC ATC TGG AGG CCT GAC  
 Gly Asp Tyr Glu Asn Val Thr Ser Ile Arg Ile Pro Ser Glu Leu Ile Trp Arg Pro Asp  
 370 390 410  
 ATC GTC CTC TAC AAC AAT GCG GAT GGA GAC TTT GCA GTC ACC CAC CTG ACC AAG GCC CAC  
 Ile Val Leu Tyr Asn Asn Ala Asp Gly Asp Phe Ala Val Thr His Leu Thr Lys Ala His  
 430 450 470  
 CTG TTC TAT GAC GGA AGG GTG CAG TGG ACA CCC CCA GCC ATC TAT AAG AGC TCC TGC AGC  
 Leu Phe Tyr Asp Gly Arg Val Gln Trp Thr Pro Pro Ala Ile Tyr Lys Ser Ser Cys Ser  
 490 510 530  
 ATC GAC GTC ACC TTC TTC CCC TTT GAC CAG CAG AAC TGT ACC ATG AAG TTT GGA TCC TGG  
 Ile Asp Val Thr Phe Phe Pro Phe Asp Gln Gln Asn Cys Thr Met Lys Phe Gly Ser Trp  
 550 570 590  
 ACC TAC GAC AAG GCC AAG ATT GAC TTA GTG AGC ATT CAT AGC CGT GTG GAC CAA CTG GAC  
 Thr Tyr Asp Lys Ala Lys Ile Asp Leu Val Ser Ile His Ser Arg Val Asp Gln Leu Asp  
 610 630 650  
 TTC TGG GAA AGT GGG GAG TGG GTC ATC GTG GAT GCT GTG GGC ACC TAC AAC ACC AGG AAG  
 Phe Trp Glu Ser Gly Glu Trp Val Ile Val Asp Ala Val Gly Thr Tyr Asn Thr Arg Lys  
 670 690 710  
 TAC GAG TGC TGT GCC GAG ATC TAT CCT GAC ATC ACC TAT GCC TTC ATC ATC CGA CGC CTG  
 Tyr Glu Cys Cys Ala Glu Ile Tyr Pro Asp Ile Thr Tyr Ala Phe Ile Ile Arg Arg Leu  
 730 750 770  
 CCG CTA TTC TAC ACC ATC AAC CTC ATC ATC CCG TGC CTG CTC ATC TCC TGT CTC ACC GTG  
 Pro Leu Phe Tyr Thr Ile Asn Leu Ile Ile Pro Cys Leu Leu Ile Ser Cys Leu Thr Val

FIG. 2A-1



790 810 830  
CTG GTC TTC TAT CTG CCT TCA GAG TGT GGC GAG AAG GTC ACA CTG TGC ATC TCG GTG CTG  
Leu Val Phe Tyr Leu Pro Ser Glu Cys Gly Glu Lys Val Thr Leu Cys Ile Ser Val Leu

850 870 890  
CTT TCT CTC ACC GTC TTC CTG CTG CTC ATC ACC GAG ATC ATC CCG TCC ACC TCG CTG GTG  
Leu Ser Leu Thr Val Phe Leu Leu Leu Ile Thr Glu Ile Ile Pro Ser Thr Ser Leu Val

910 930 950  
ATC CCG CTC ATC GGC GAG TAC CTC CTC TTC ACC ATG ATC TTC GTC ACC CTC TCC ATC GTG  
Ile Pro Leu Ile Gly Glu Tyr Leu Leu Phe Thr Met Ile Phe Val Thr Leu Ser Ile Val

970 990 1010  
ATC ACG GTC TTC GTG CTC AAT GTG CAC CAC CCG TCG CCA CGC ACA CAC ACG ATG CCC GGC  
Ile Thr Val Phe Val Leu Asn Val His His Arg Ser Pro Arg Thr His Thr Met Pro Ala

1030 1050 1070  
TGG GTG CGT AGA GTC TTC CTG GAC ATC GTG CCT CGC CTC CTC TTC ATG AAG CGC CCC TCT  
Trp Val Arg Arg Val Phe Leu Asp Ile Val Pro Arg Leu Leu Phe Met Lys Arg Pro Ser

1090 1110 1130  
GTG GTC AAA GAC AAC TGC CGG AGA CTT ATT GAG TCC ATG CAC AAG ATG GCC AAC GCC CCC  
Val Val Lys Asp Asn Cys Arg Arg Leu Ile Glu Ser Met His Lys Met Ala Asn Ala Pro

1150 1170 1190  
CGC TTC TGG CCA GAG CCT GTG GGC GAG CCC GGC ATC TTG AGT GAC ATC TGC AAC CAA GGT  
Arg Phe Trp Pro Glu Pro Val Gly Glu Pro Gly Ile Leu Ser Asp Ile Cys Asn Gln Gly

1210 1230 1250  
CTG TCA CCT GCC CCA ACT TTC TGC AAC CCC ACG GAC ACA GCA GTC GAG ACC CAG CCT ACG  
Leu Ser Pro Ala Pro Thr Phe Cys Asn Pro Thr Asp Thr Ala Val Glu Thr Gln Pro Thr

1270 1290 1310  
TGC AAG TCA CCC CCC CTT GAG GTC CCT GAC TTG AAG ACA TCA GAG GTT GAG AAG GCC AGT  
Cys Arg Ser Pro Pro Leu Glu Val Pro Asp Leu Lys Thr Ser Glu Val Glu Lys Ala Ser

1330 1350 1370  
CCC TGT CCA TCG CCT GGC TCC TGT CCT CCA CCC AAG AGC AGC AGT GGG GCT CCA ATG CTC  
Pro Cys Pro Ser Pro Gly Ser Cys Pro Pro Pro Lys Ser Ser Ser Gly Ala Pro Met Leu

1390 1410 1430  
ATC AAA GCC AAG TCC CTG AGT GTC CAG CAT GTG CCC AGC TCC CAA GAA GCA GCA GAA GAT  
Ile Lys Ala Arg Ser Leu Ser Val Gln His Val Pro Ser Ser Gln Glu Ala Ala Glu Asp

1450 1470 1490  
GGC ATC CCG TGC CGG TCT CGG AGT ATC CAG TAC TGT GTT TCC CAA GAT GGA GCT GCC TCC  
Gly Ile Arg Cys Arg Ser Arg Ser Ile Gln Tyr Cys Val Ser Gln Asp Gly Ala Ala Ser

1510 1530 1550  
CTG GCT GAC AGC AAG CCC ACC AGC TCC CCG ACC TCC CTG AAG GCC CGT CCA TCC CAG CTT  
Leu Ala Asp Ser Lys Pro Thr Ser Ser Pro Thr Ser Leu Lys Ala Arg Pro Ser Gln Leu

FIG.2A-2



1570 1590 1610  
CCC GTG TCA GAC CAG GCC TCT CCA TGC AAA TGC ACA TGC AAG GAA CCA TCT CCT GTG TCC  
Pro Val Ser Asp Gln Ala Ser Pro Cys Lys Cys Thr Cys Lys Glu Pro Ser Pro Val Ser

1630 1650 1670  
CCA GTC ACT GTG CAC AAG GCG GGA GGC ACC AAA GCA CCT CCC CAA CAC CTG CCC CTG TCA  
Pro Val Thr Val Leu Lys Ala Gly Gly Thr Lys Ala Pro Pro Gln His Leu Pro Leu Ser

1690 1710 1730  
CCA GCC CTG ACA CGG GCA GTA GAA GGC GTC CAG TAC ATT GCA GAC CAC CTC AAG GCA GAA  
Pro Ala Leu Thr Arg Ala Val Glu Gly Val Gln Tyr Ile Ala Asp His Leu Lys Ala Glu

1750 1770 1790  
GAC ACT GAC TTC TCG GTG AAG GAG GAC TGG AAA TAC GTG GCC ATG GTC ATT GAC CGA ATC  
Asp Thr Asp Phe Ser Val Lys Glu Asp Trp Lys Tyr Val Ala Met Val Ile Asp Arg Ile

1810 1830 1850  
TTC CTC TGG ATG TTC ATC ATT GTC TGC CTT CTG GGC ACT GTG GGA CTC TTC CTG CCT CCC  
Phe Leu Trp Met Phe Ile Ile Val Cys Leu Lue Gly Thr Val Gly Leu Phe Leu Pro Pro

1870 1890 1917  
TGG CTG GCT GCT TGC TGA TGGCTTCGACAGTGTCTCAGGCTCACGTCTCTGCTGACTTTGTTCCCGAG  
Trp Leu Ala Ala Cys

1943 1969 1997  
TTTCTTCTCCGACAAAGTTGGCCTCCCTTCATTTATTCCTGTTATTTTGGGCTTCGTGTTATTAATATCCTTCCCTGCC  
TCTGTGGCGCATTGTAAGTTTTAAAAATTAATAGACCAAAGCC...3'

2022 2048  
TCTGTGGCGCATTGTAAGTTTTAAAAATTAATAGACCAAAGCC...3'

4-2 cDNA: 3' end

1867 1884 1912  
CCC TGG CTG GCT GGT ATG ATC TAG GGACGTGGTGGTGCCAGCTCCACATCTCTGTAGGGCCATAC  
Pro Trp Leu Ala Gly Met Ile

1937 1963 1991  
GACTCGTCAGTCACCCACATCTTCCAAACCGGCTGACCATGAGACACCCTAGGAGAGAGATGATGCTTCTTGGGAGATG

2016 2042 2070  
GAAGTTGGCCCTGTTCTAGTCAGACTATGGGCGTGGTTGGAGAGAAATGAGGGCTGATACAGTTGCAGGCCGAGTCCC

2095 2121 2149  
CATTAAAGTTTCTCCAGAGCAAGTGGCAGTACTCCCTGACTTACAGACAGCACACCCATCTGTGTACAGAGAATGA

2174 2200 2228  
TCCCGAGTTGATCTCAGTTGCTCTTTGAGGCCATGAAAAATTCATCCACCTTGAGGAACAGAGCCTCTCATGCTGTGG

2253 2279 2307  
GATCAATAAGACAGGAATCTCCCACTGTGACTCTGCTGGCCACACCCTCTCCCTCCCAAGAAGTGGTCCCTCATCC  
CCCAATTC...3'

FIG.2A-3

ATAAAGTCTCCGGCAGTTGTCTTTTGACCACAGAGGGACGAGCGCGCGCAGCTCTGGAGCGGAGGGCGGGCAGACAGCGGGCGAGCCGCCGCA  
-210 -180 -150 -120

[illegible]

**FIG. 2B-1**

Asp	Phe	Trp	Glu	Ser	180	Glu	Trp	Val	Ile	Val	Ile	Asp	Ala	Val	Gly	Thr	Asn	Thr	Arg	Lys	Tyr	Glu	Cys	200	Glu	Ile	Tyr	Pro	
GAC	TTC	TGG	GAA	AGT	540	GAG	TGG	GTC	ATC	GTG	GAT	GCT	GTG	GGC	ACC	TAC	AAC	ACC	AGG	AAG	TAC	GAG	TGT	600	GAG	ATC	TAT	CCT	
Asp	Ile	Thr	Tyr	Ala	210	Ile	Ile	Arg	Arg	Leu	Pro	Leu	Phe	Thr	Tyr	Thr	Asn	Leu	Ile	Ile	Pro	Cys	Leu	230	Ser	Cys	Leu	Thr	
GAC	ATC	ACC	TAT	GCC	630	ATC	ATC	CGA	CGC	CTG	CCG	CTA	TTC	TAC	ACC	ATC	AAC	CTC	ATC	ATC	CCG	TGC	CTG	690	TCC	TGT	CTC	ACC	
Val	Leu	Val	Phe	Tyr	240	Pro	Ser	Glu	Cys	Gly	Gly	Lys	Val	Thr	Leu	Cys	Ile	Ser	Val	Leu	Leu	Ser	Leu	260	Phe	Leu	Leu	Leu	
GTG	CTG	GTC	TAT	TTC	720	CTG	TCA	GAG	TGT	GGC	GAG	AAG	GTC	ACA	CTG	TGC	ATC	TCC	GTC	CTT	CTT	TCT	CTC	780	TTC	CTG	CTG	CTC	
Ile	Thr	Glu	Ile	Ile	270	Ser	Thr	Ser	Leu	Val	Ile	Pro	Leu	Ile	Gly	Gly	Tyr	Leu	Leu	Phe	Thr	Met	Ile	290	Thr	Leu	Ser	Ile	
ATC	ACC	GAG	ATC	ATC	810	TCC	ACC	TCC	CTG	ATC	ATC	CCG	CTC	ATC	GGC	GAG	TAC	CTC	CTC	TTC	ACC	ATG	ATC	870	ACC	CTC	TCC	ATC	
Val	Ile	Thr	Val	Phe	300	Leu	Asn	Val	His	His	Arg	Ser	Pro	Arg	Thr	His	Thr	Met	Pro	Ala	Irp	Val	Arg	320	Phe	Leu	Asp	Ile	
GTG	ATC	ACG	GTC	TTC	900	CTC	AAT	GTG	CAC	CAC	CGC	TGC	CCA	CGC	ACA	CAC	ACG	ATG	CCC	CCC	TGG	GTG	CGT	AGA	960	TTC	CTG	GAC	ATC
Val	Pro	Arg	Leu	Leu	330	Met	Lys	Arg	Pro	Ser	Val	Val	GTC	AAA	GAC	Cys	Arg	Arg	Leu	Ile	Glu	Ser	Met	350	Met	Ala	Asn	Ala	
GTG	CCT	CGC	CTC	CTC	990	ATG	AAG	CGC	CCC	TCT	GTG	GTG	ATC	GGC	AAA	TGC	CGG	AGA	CTT	ATT	GAG	TCC	ATG	1050	ATG	GCC	AAC	GCC	
Pro	Arg	Phe	Trp	Pro	360	Pro	Val	Gly	Glu	Pro	Gly	Ile	Leu	Ser	Asp	Ile	Cys	Asn	Gln	Gly	Leu	Ser	Pro	380	Thr	Phe	Cys	Asn	
CCC	CGC	TTC	TGG	CCA	1080	CGC	GTG	GGC	GAG	CCC	GGC	ATC	TTG	AGT	GAG	ATC	TGC	AAC	CAA	GGT	CTG	TCA	CCT	1140	ACT	TTC	TGC	AAC	
Pro	Thr	Asp	Thr	Ala	390	Glu	Thr	Gln	Pro	Thr	Cys	Arg	Ser	Pro	Pro	Leu	Glu	Val	Pro	Asp	Leu	Lys	Thr	410	Val	Glu	Lys	Ala	
CCC	ACG	GAC	ACA	GCA	1170	GTG	GAG	ACC	CAG	CCG	TGC	AGG	TCA	CCC	CCC	CTT	GAG	GTC	CCT	GAC	TTG	AAG	ACA	1230	GTT	GAG	AAG	GCC	

**FIG. 2B-2**

[illegible]

**FIG. 2B-3**

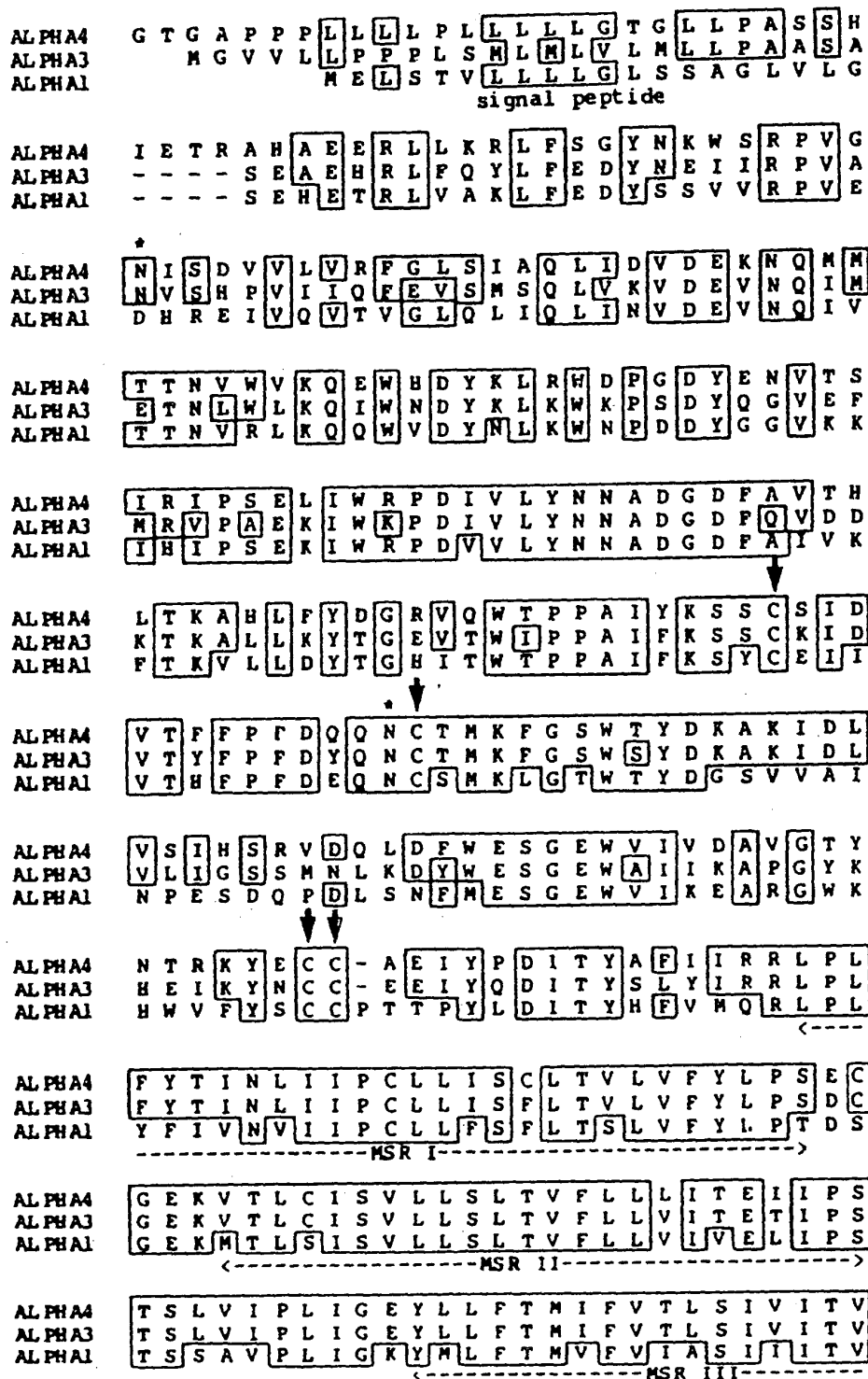


FIG.3A





ALPHA4 F V L N V H H R S P R T H T M P A W V R R V F L D I V  
ALPHA3 F V L N V H Y R T P T T H T M P T W V K A V F L N L L  
ALPHA1 I V I N T H H R S P S T H I M P E W V R K V F I D T I  
----->

ALPHA4 P R L L F - - - M K R P S V V K D N C R R L I E S M H  
ALPHA3 P R V M F - - - M T R P T S G E G D T P K T - - - -  
ALPHA1 P N I M F F S T M K R P S R D K Q E K R I F - - - -

ALPHA4 K M A N A P R F W P E P V G E P G I L S D I C N Q G L  
ALPHA3 - - - - - - - - - - R T F Y G A E L S N L N C F S R  
ALPHA1 - - - - - - - - - - T E D I D I S D I S G K P G

ALPHA4 S P A P T F C N P T D T A V E T Q P T C R S P P L E V  
ALPHA3 A D S K S C K E G Y P C Q D G T C G Y C H H R R V K I  
ALPHA1 P P P M G F H - - - - - - - - - - - - - - - - - -

ALPHA4 P D L K T S E V E K A S P C P S P G S C P P P K S S S  
ALPHA3 S N F - - - - - - - - - - - - - - - - - - S A N L T R S S S  
ALPHA1 -

ALPHA4 G A P M L I K A R S L S V Q H V P S S Q E A A E D G I  
ALPHA3 S E S V - - - - - - - - - - - - - - - - - -  
ALPHA1 -

ALPHA4 R C R S R S I Q Y C V S Q D G A A S L A D S K P T S S  
ALPHA3 -  
ALPHA1 -

ALPHA4 P T S L K A R P S Q L P V S D Q A S P C K C T C K E P  
ALPHA3 -  
ALPHA1 -

ALPHA4 S P V S P V T V L K A G G T K A P P Q H L P L S P A L  
ALPHA3 - - - - - - - - - - - - - - - - - - N A V L S L S A L S P E I  
ALPHA1 - - - - - - - - - - - - - - - - - - S P L I K H P E V  
-----<

ALPHA4 T R A V E G V Q Y I A D H L K A E D T D F S V K E D W  
ALPHA3 K E A I Q S V K Y I A E N M K A Q N V A K E I Q D D W  
ALPHA1 K S A I E G V K Y I A E T M K S D Q E S N N A A E E W  
amphipathic helix----->

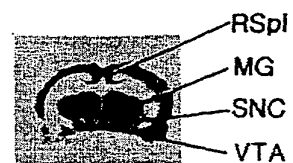
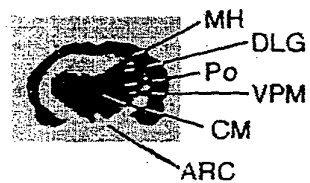
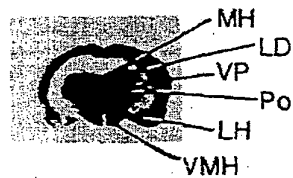
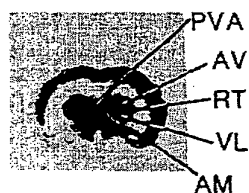
ALPHA4 K Y V A M V I D R I F L W M F I I V C L L G T V G L F  
ALPHA3 K Y V A M V I D R I F L W V F I L V C I L G T A G L F  
ALPHA1 K Y V A M V M D H I L L G V F H L V C L I G T L A V F  
-----<-----MSR IV----->

ALPHA4 L P P W L A G M I  
ALPHA3 L Q P L M A - R D D T  
ALPHA1 A G R L I E L H Q Q G  
----->

FIG.3B

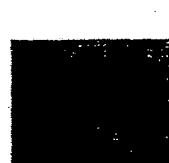
**FIG.4A**

Clone 4-1;  
Antisense



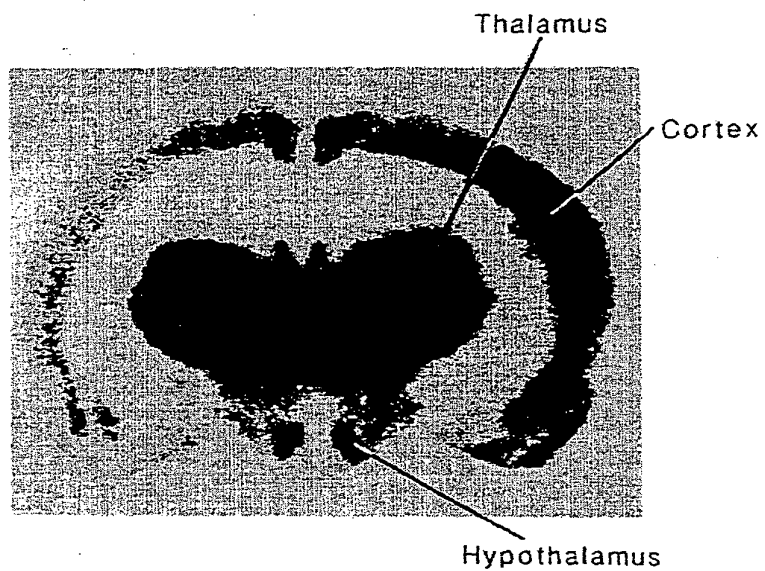
**FIG.4B**

Clone 4-1;  
Sense



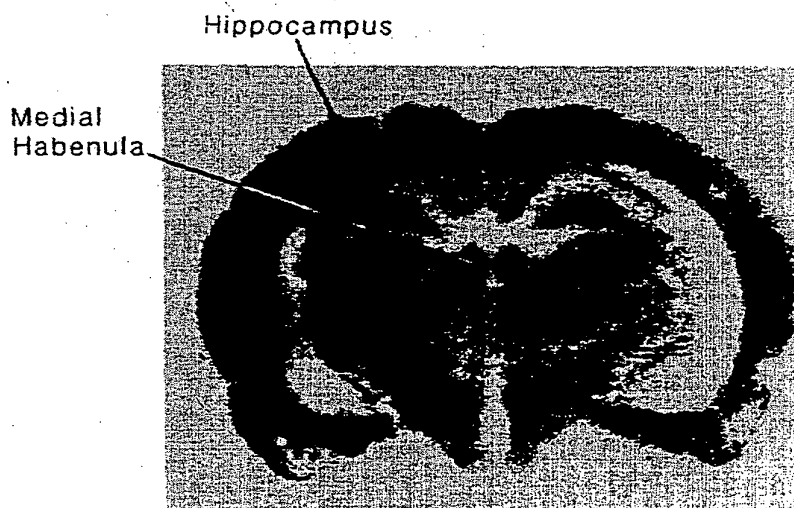


**FIG.5A**



PROBE: Alpha 4

**FIG.5B**



PROBE: Alpha 3

FIG.6A

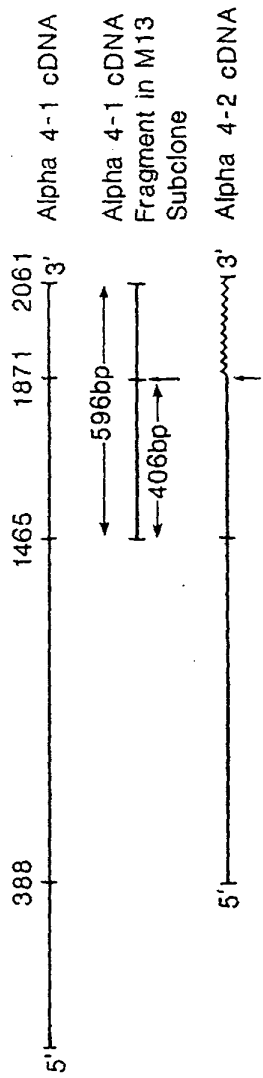


FIG.6B

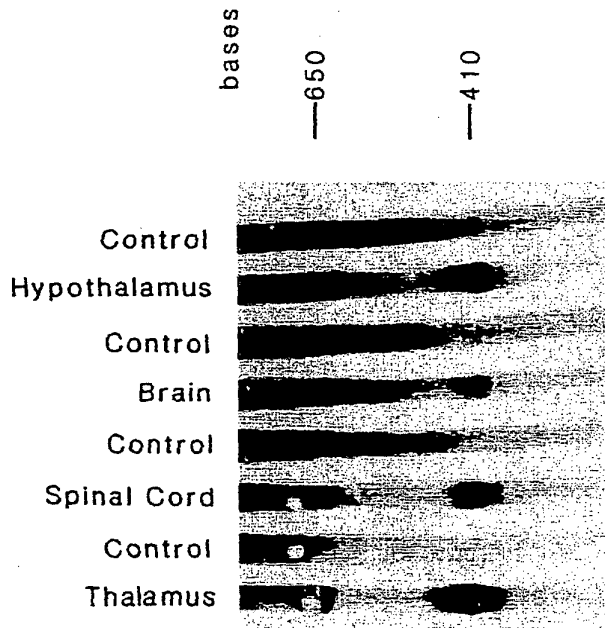
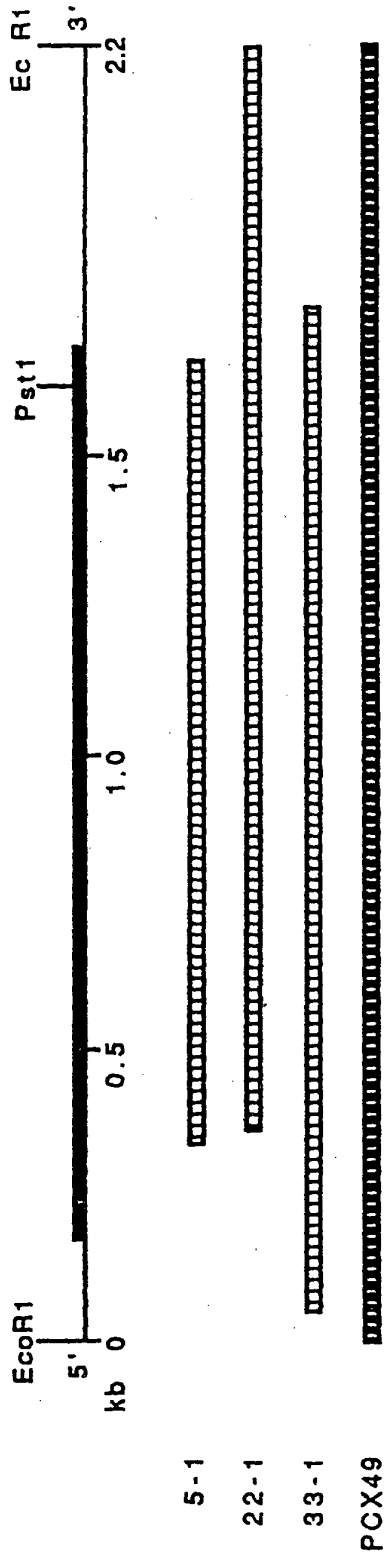




FIG.7A





5' ..... -179 -100  
GGGGAACACACCGGGACCGGCAAGAAGCCGGGACCTCCCTCGTTGCAGGAACCTGCCCGTTTCAGTGAGCACTTTAGACC  
TGGAGGCCGGAGCCCGGACCCCGGAGCGGGCTGCGGGCTTCAGCACCGGACGCGCTCGACCCGCGAGCCCTAGTATCCGAGAGGCTGCGCGCT  
ATG CTG GCT TGC ATG GCC GGG CAC TCC AAC TCA ATG GCG CTG TTC AGC TTC AGC CTT CTT TGG CTG TGC TCA GGG  
Met Leu Ala Cys Met Ala Gly His Ser Asn Ser Met Ala Leu Phe Ser Phe Ser Leu Leu Trp Leu Cys Ser Gly  
1 60  
GTT TTG GGA ACT GAC ACA GAG GAG CGG CTA GTG GAG CAT CTC TTA GAT CCC TCC CGC TAT AAC AAG CTG ATT CGT  
Val Leu Gly Thr Asp Thr Glu Glu Arg Leu Val Glu His Leu Leu Asp Pro Ser Arg Tyr Asn Lys Leu Ile Arg  
26 90  
CCA GCT ACT AAC GGC TCT GAG CTG GTG ACT GTA CAG CTC ATG GTA TCA TTG GCT CAG CTC ATT AGT GTG CAC GAG  
Pro Ala Thr Asn Gly Ser Glu Leu Val Thr Val Glu Leu Met Val Ser Leu Ala Gln Leu Ile Ser Val His Glu  
51 180  
CGG GAG CAG ATC ATG ACC ACC AAT GTC TGG CTG ACC CAG GAG TGG GAA GAT TAC CGC CTC ACA TGG AAG CCT GAG  
Arg Glu Gln Ile Met Thr Thr Asn Val Trp Leu Thr Gln Glu Trp Glu Asp Tyr Arg Leu Thr Trp Lys Pro Glu  
76 240  
GAC TTC GAC AAT ATG AAG AAA GTC CGG CTC CCT TCC AAA CAC ATC TGG CTC CCA GAT GTG GTT CTA TAC AAC AAT  
Asp Phe Asp Asn Met Lys Lys Val Arg Leu Pro Ser Lys His Ile Trp Leu Pro Asp Val Val Leu Tyr Asn Asn  
101 330  
GCT GAC GGC ATG TAC GAA GTC TCC TTC TAT TCC AAT GCT GTG GTC TCC TAT GAT GGC AGC ATC TTT TGG CTA CCA  
Ala Asp Gly Met Tyr Glu Val Ser Phe Tyr Ser Asn Ala Val Val Ser Tyr Asp Gly Ser Ile Phe Trp Leu Pro  
126 390  
CCT GCC ATC TAC AAG AGT GCA TGC AAG ATT GAG GTG AAG CAC TTC CCA TTT GAC CAG AAT TGC ACC ATG AAG  
Pro Ala Ile Tyr Lys Ser Ala Cys Lys Ile Glu Val Lys His Phe Pro Phe Asp Gln Gln Asn Cys Thr Met Lys  
151 480

FIG.7B-1



540  
TTT CGC TCA TGG ACC TAC GAC CGT ACT GAG ATT GAC CTG GTG CTC AAA AGT GAT GTG GCC AGT CTG GAT GAC TTC  
Phe Arg Ser Trp Thr Thr Asp Tyr Asp Arg Thr Glu Thr Glu Ile Asp Leu Val Val Leu Lys Ser Asp Val Ala Ser Leu Asp Asp Phe  
176

630  
ACA CCC AGC GGG GAG TGG GAC ATC ATC GCA CGC CGA GGC CCA CTG CCA AAC GAG AAC CCA GAC GAC TCC ACC TAT GTG  
Thr Pro Ser Gly Glu Glu Trp Asp Ile Ile Ala Leu Pro Gly Arg Arg Asn Glu Asn Pro Asp Asp Ser Thr Tyr Val  
201

690  
GAC ATC ACC TAT GAC TTC ATC ATT CGT CGC AAA CCA CTC TTC TAC ACT ATC AAC CTC ATC CCC TGC GTA CTC  
Asp Ile Thr Tyr Asp Phe Ile Ile Arg Arg Arg Lys Pro Leu Phe Tyr Thr Ile Asn Leu Ile Ile Pro Cys Val Leu  
226

780  
ATC ACC TCG CTG GCC ATC CTG GTC TTC TAC TCG CCC TCA GAC TGT GGT GAA AAG ATG ACA CTT TGT ATT TCT GTG  
Ile Thr Ser Leu Ala Ile Leu Val Phe Tyr Tyr Cys Asp Cys Gly Glu Lys Met Thr Leu Cys Ile Ser Val  
251

840  
CTG CTA GCA CTC ACG GTG TTC CTG CTC ATC TCC AAG ATT GTG CCT CCC ACC TCC CTC GAT GTA CCG CTG GTG  
Leu Leu Ala Leu Thr Thr Phe Val Val Leu Leu Ile Ser Lys Ile Val Val Ser Leu Asp Val Pro Leu Val  
276

930  
GGC AAG TAC CTC ATG TTT ACC ATG GTG CTA GTC ACC TTC TCC ATC ATC ACC AGC GTG TGT GTG CTC AAT GTG CAC  
Gly Lys Tyr Leu Met Phe Thr Met Val Leu Leu Val Thr Phe Ser Ile Val Thr Ser Val Cys Val Leu Asn Val His  
301

990  
CAC CGC TCG CCT ACC ACG CAC ACC ATG GCC CCC TGG GTC AAG GTG GTC TTC CTG GAG AAG CTG CCC ACC CTG CTC  
His Arg Ser Pro Thr Thr His Thr Met Ala Pro Trp Val Lys Val Val Phe Leu Glu Lys Leu Pro Thr Leu Leu  
326

1080  
TTC CTG CAG CAG CCA CGC CAC CGC TGT GCA CGT CAG CGT CTG CGC TTG AGG AGG CGC CAG CGA GAG CGT GAG GGC  
Phe Leu Gln Gln Pro Arg Arg His Arg Cys Ala Arg Gln Arg Leu Arg Arg Arg Gln Arg Glu Arg Glu Gly  
351

570  
720  
810  
870  
960  
1020  
1110

FIG.7B-2



1140  
GAG GCG GTT TTC TTC CGT GAA GGT CCT GCG GCT GAC CCA TGT ACC TGC TTT GTC AAC CCT GCA TCA GTG CAG GGC 1200  
Glu Ala Val Phe Phe Phe Arg Glu Gly Pro Ala Ala Asp Pro Cys Thr Cys Phe Val Asn Pro Ala Ser Val Gln Gly  
376

1230  
TTG GCT GGG GCT TTC CGA GCT GAG CCC ACT GCA GCC GGC CCG GGG CGC TCT GTG GGG CCA TGC AGC TGT GGC CTC 1260  
Leu Ala Gly Ala Phe Arg Ala Glu Pro Thr Ala Ala Glu Pro Gly Arg Ser Val Gly Pro Cys Ser Cys Gly Leu  
401

1290  
CGG GAA GCA GTG GAT GGC GTA C6C TTC ATT GCG GAC CAC ATG CGA AGT GAG GAT GAT GAC CAG AGT GTG AGG GAG 1350  
Arg Glu Ala Val Asp Gly Val Arg Phe Ile Ala Asp His Met Arg Ser Glu Asp Asp Asp Gln Ser Val Arg Glu  
426

1380  
GAC TGG AAA TAC GTT GCC ATG GTG ATC GAC CGC CTG TTC CTG TGG ATC TTT GTC TTT GTC TGT GTC TTT GGG ACC 1410  
Asp Trp Lys Tyr Val Ala Met Val Ile Asp Arg Leu Phe Phe Val Phe Val Phe Val Cys Val Phe Gly Thr  
451

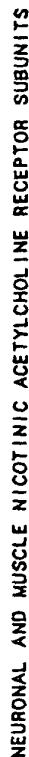
1440  
GTC GGC ATG TTC CTG CAG CCT CTC TTC CAG AAC TAC ACT GCC ACT ACC TTC CTC CAC CCT GAC CAC TCA GCT CCC 1500  
Val Gly Met Phe Leu Gln Pro Leu Phe Gln Asn Tyr Thr Ala Thr Thr Phe Leu His Pro Asp His Ser Ala Pro  
476

1596  
AGC TCC AAG TGAGGTCTCATTTCATTTGCAGCTCCTCACCCCGTGACCCCTGCGGTTTCAGTACTGGGTGCAAGATGGATCTCTCCCCACTCCACTGA 1596  
Ser Ser Lys

1695  
AGCCTGCTTCACACCTCCGTTACACATAGTCCTCCAGCCTGGAGGCTGGACCCGCTGCCCTTGTTGTCGAGCCTTCTCCTTCCCTCTGAGCTGTTCA 1695  
GGCAGGAGTGCCCAATGGTGGGGCCACGGCTGGTAAGTAGAGGCCAGAGATCACAGAGCCACCTACCCCGATGAGGTGCTGGAGAAGCGGCCCAAGAAAG 1794  
AGACAGAGTTATCTGTGACCTCCAAGTCATCGGAGAGGAGGAGGTAGGATAAGGGGCTCAGACTCTGGCAGAGTGC6GCTAGTACTTGGCGCCCAACCA 1893  
CTTAAGTGAGCGACACTGGTCTGGGAGGACTCGAAGTGTGGGGAGCTCTCTTTGGGAGCTCGGTCTCCCCACCCCTGTACCTCAGAGGGGCTCCAGACCCCGG 1992  
2017  
GCTTCAGGTTCCCTTCTGCCAGTGC.....3'

FIG.7B-3





KKVRLD SKHILPWLVTHRRMGVYEVSYFNVAVYDSS IEWPPALYR SACKLEVKHFPFDRGRCIMKTPSWITDRTEDLVLKSDVASLODQTPSGIWDJIALPG  
 TSIRHISELWRPULVYNNAGDFANTHLTKAHLFTFOORVQVITPPATYXSXSSIDVTFPFYDQRCIMKTSWITDCAKJDLVYSIHSRVDOLOFWESGIWGVNVDVAG  
 EFWBPAEKKWKPJLVIYRRAGDFDNDRTKALKKLTBEVTHLEPPALFYSSKSDVITYPFYDQRCIMKTSWITDCAKJDLVYSIHSRVDOLOFWESGIWGVNVDVAG  
 KKIHIPSEKWRPQWLVTHRRAGDFVIVKFTKVLDDTHITHTWTPPAIFXSCELVTHLEHPTDEGRCSAKLGTWITDYGSVVAINPESDOPDLSNFMSGIWVWIKKEARG

[illegible][illegible]

LEVPDLKTSEVEKASCPSPGSCPPPKSSGAPMLIKARLSVQHVPPSSQEAEDGIRCRSRSLQYCVSQDGAASLADSKPTSSPTSLIKARPSQLPVSDOASPKCTC  
CYTODI ASUIC REGION

ASVOGLAGAFRAEPTAAGPGRSVGPCGGLREAVDGGRRFADHMRSEDDDDQSVREHWKLVAKVKTDRITWLVFVGVFVIVVAVTQQLFQNYTATTFELHPDHSAPSSK  
KEPSPVSPVTLKAGGTAKPQPHLPLSPALTRAVEGQYQDHLKAEDTDFSVKEHWKLVAKVKTDRITWLVFVGVFVIVVAVTQQLFQNYTATTFELHPDHSAPSSK  
ISNFSAANLTRSSSESNAVLNLSLSALSPKEMIQSQKYDENKKAQNVAKEIQDHWKLVAKVKTDRITWLVFVGVFVIVVAVTQQLFQNYTATTFELHPDHSAPSSK  
TEDIDISDISGKPGPPPMGFGHSPLIKHPEVKSLEGKYDETMSQDQESNNAAAEHWKLVAKVKTDRITWLVFVGVFVIVVAVTQQLFQNYTATTFELHPDHSAPSSK

**Fig. 8**



FIG.9A

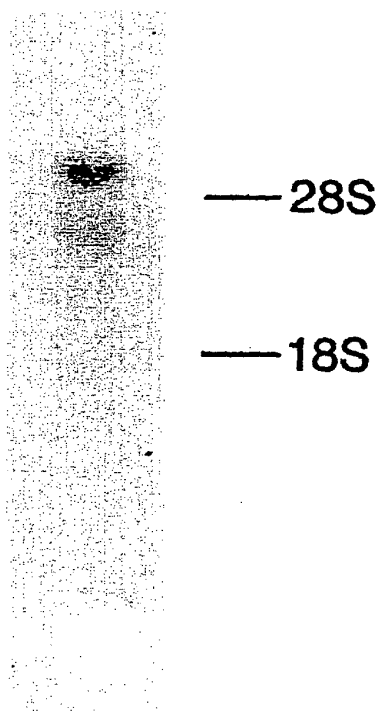
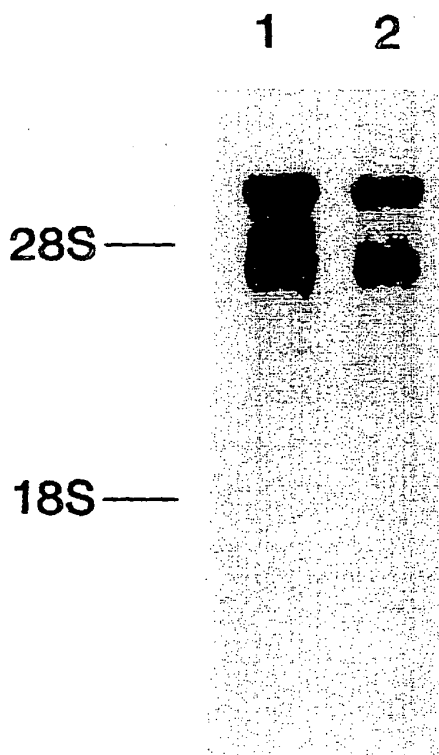
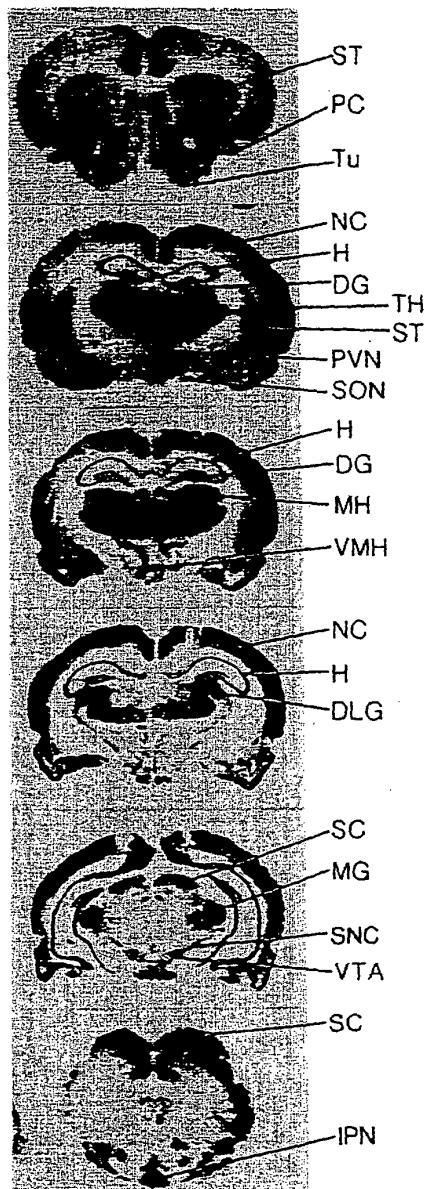


FIG.9B





**FIG. 10A**  
ANTISENSE



**FIG. 10B**  
SENSE





ALPHA-SUBUNIT COMPARISON

ALPHA 1 MELSTVLLGLSSAGLVGSEHTNTNAKLEDESSVVRHDEHREIPQVTGLQLPDIKXDIYDQIVTIRVRLKQDQVVDNKKXNDIDGGCKIHIPS  
ALPHA 3 MGVVLLPPLSLMLVLMKLLPAASAEAHUIFOYIEDNEIIRPVANVSHPIIQFEVSHSGLEKVKQDFVQDINEQLWLKGIAMVXKXKXSDVQCGEFMRVDA  
ALPHA 4 MANGSGAPPPLLLPLLLLTGQLPASPASHTETRAKAEMLKRLSGKRWSSHNGNISDVLVRFGLSIADLIQDQIQQDMMNTIRVVYKDEMDYKTRDQCDTENVTISIRIQS  
SIGNAL PEPTIDE

ALPHA 1 EKTRPDVLTTHRDGDAIIVKFKVLTDTTHITTPPAIFKSYCEIETINPTDEQDSMAITMIGGSVVAINPESDOPDLSNFMESGEMKERRGNKHWVFISGPTTPTL  
ALPHA 3 EKTRPDVLTTHRDGDAIIVKFKVLTDTTHITTPPAIFKSYCEIETINPTDEQDSMAITMIGGSVVAINPESDOPDLSNFMESGEMKERRGNKHWVFISGPTTPTL  
ALPHA 4 ELKTRPDVLTTHRDGDAIIVKFKVLTDTTHITTPPAIFKSYCEIETINPTDEQDSMAITMIGGSVVAINPESDOPDLSNFMESGEMKERRGNKHWVFISGPTTPTL  
ACETYLCHOLINE

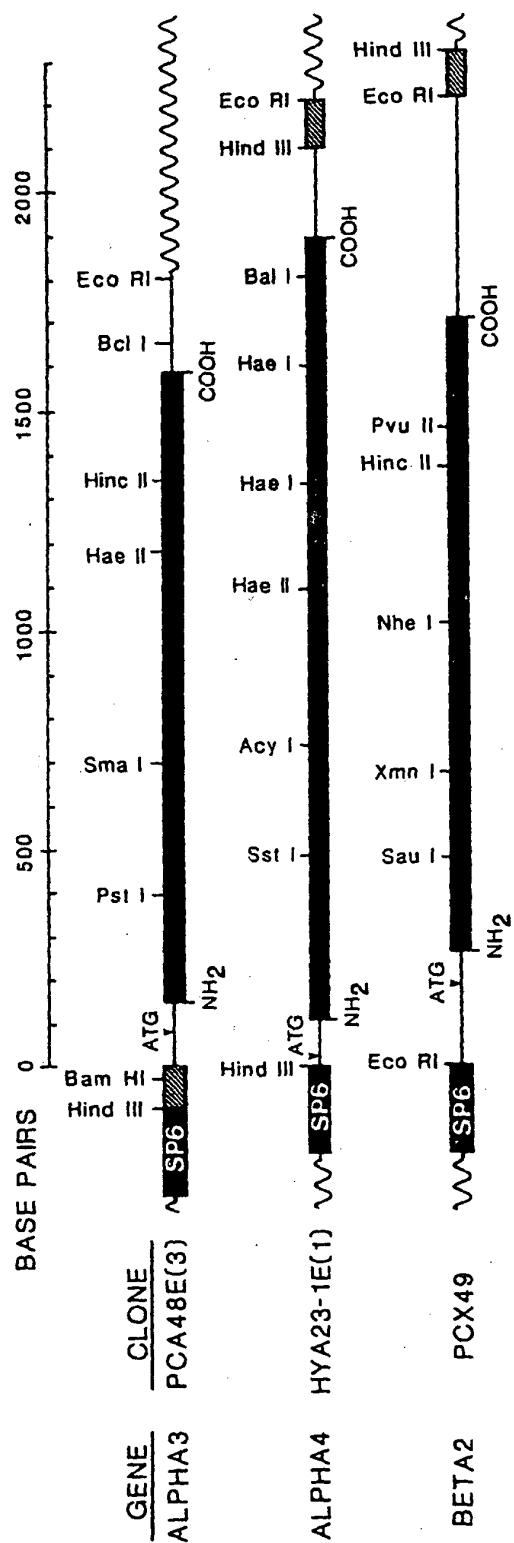
ALPHA 1 DITLHFVMDRIIVFIVVTPGLTFHFISVPTITPTOSMKTSSSVLLSTIXLLIVMLPSTSSAVPLTCKAGCTMVVIAIIPVIVITITTHISSEHIMHWRKVF  
ALPHA 3 DITLHFVMDRIIVFIVVTPGLTFHFISVPTITPTOSMKTSSSVLLSTIXLLIVMLPSTSSAVPLTCKAGCTMVVIAIIPVIVITITTHISSEHIMHWRKVF  
ALPHA 4 DITLHFVMDRIIVFIVVTPGLTFHFISVPTITPTOSMKTSSSVLLSTIXLLIVMLPSTSSAVPLTCKAGCTMVVIAIIPVIVITITTHISSEHIMHWRKVF  
MEMBRANE SPANNING I MEMBRANE SPANNING II MEMBRANE SPANNING III

ALPHA 1 IDTIRNIMFSTMKRPSRDKQKRIFTEDIDISDLSGKGGPPHGFH  
ALPHA 3 LNLIRVMTATRPISGEGDTPKTRTFYGAELSNLACFSRADSKCKEGYPCDDGTCGYCHRRRVKISNFSANLTRSSSESSEVNAV  
ALPHA 4 LDIVIRLLAKRPSVVKNCRRLLIESHKMANAPRFWPEVGPGLISDICHQGLSPAPTFCNPTDTAVETOPTCRSPPLEVPDLKTSEVEKASPCPSGSCPPPKSSSGAPMLIXA  
CYTOPLASMIC REGION

ALPHA 1 RSLSVQHVPSSQEAEDGIKCRSRSIOYCVSDGGAASLADSKPTSSPTSLKARPSOLPVSDQASPCCKCTCKEPPSPVTVLKAGGTKAPPOHPLSL  
ALPHA 3 RSLSVQHVPSSQEAEDGIKCRSRSIOYCVSDGGAASLADSKPTSSPTSLKARPSOLPVSDQASPCCKCTCKEPPSPVTVLKAGGTKAPPOHPLSL  
ALPHA 4 RSLSVQHVPSSQEAEDGIKCRSRSIOYCVSDGGAASLADSKPTSSPTSLKARPSOLPVSDQASPCCKCTCKEPPSPVTVLKAGGTKAPPOHPLSL  
AMPHIPATHIC HELIX

ALPHA 1 QESNNAAEKSTSSVLLGLVAVAGRLIELHOOG  
ALPHA 3 NVAKEIGDDVAVVILGLVAVAGRLIELHOOG  
ALPHA 4 DTDFSVKEDVAVVILGLVAVAGRLIELHOOG  
MEMBRANE SPANNING IV

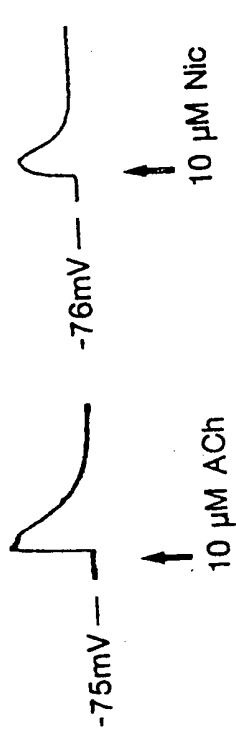
FIG.11



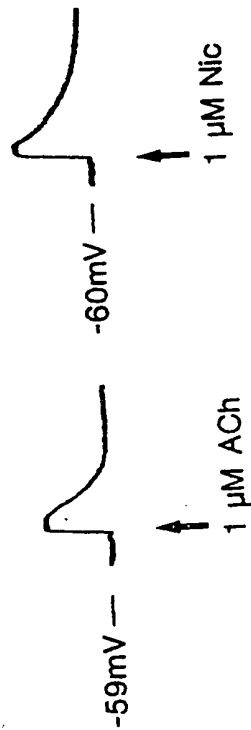
Responses to  
Nicotine (Nic)

Responses to  
Acetylcholine (ACh)

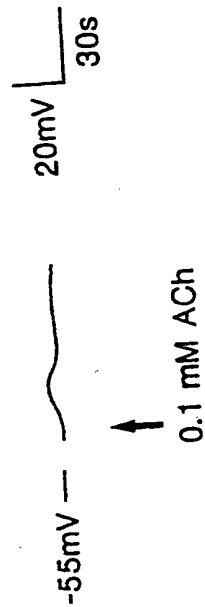
mRNAs  
injected



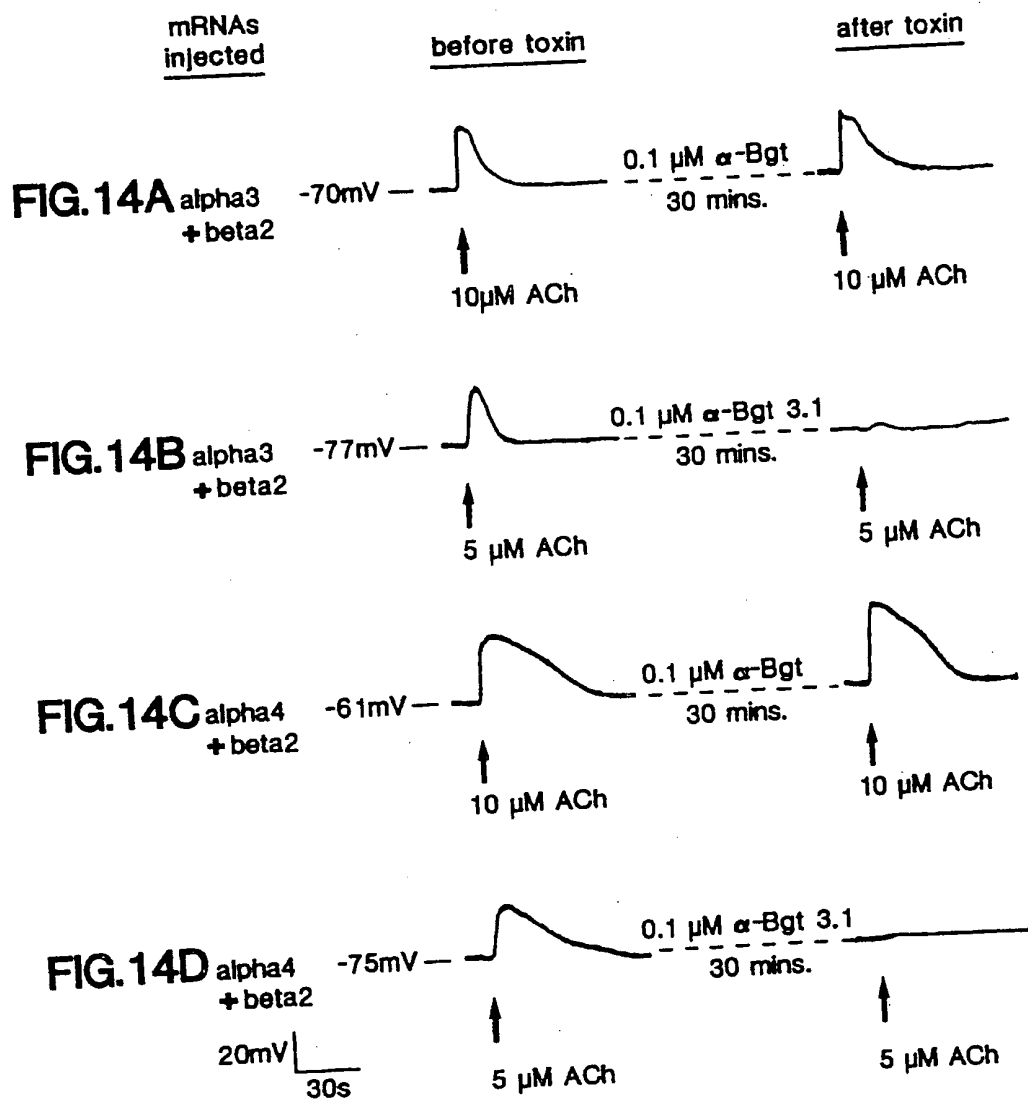
**FIG.13A** alpha3  
+ beta2



**FIG.13B** alpha4  
+ beta2



**FIG.13C** alpha4



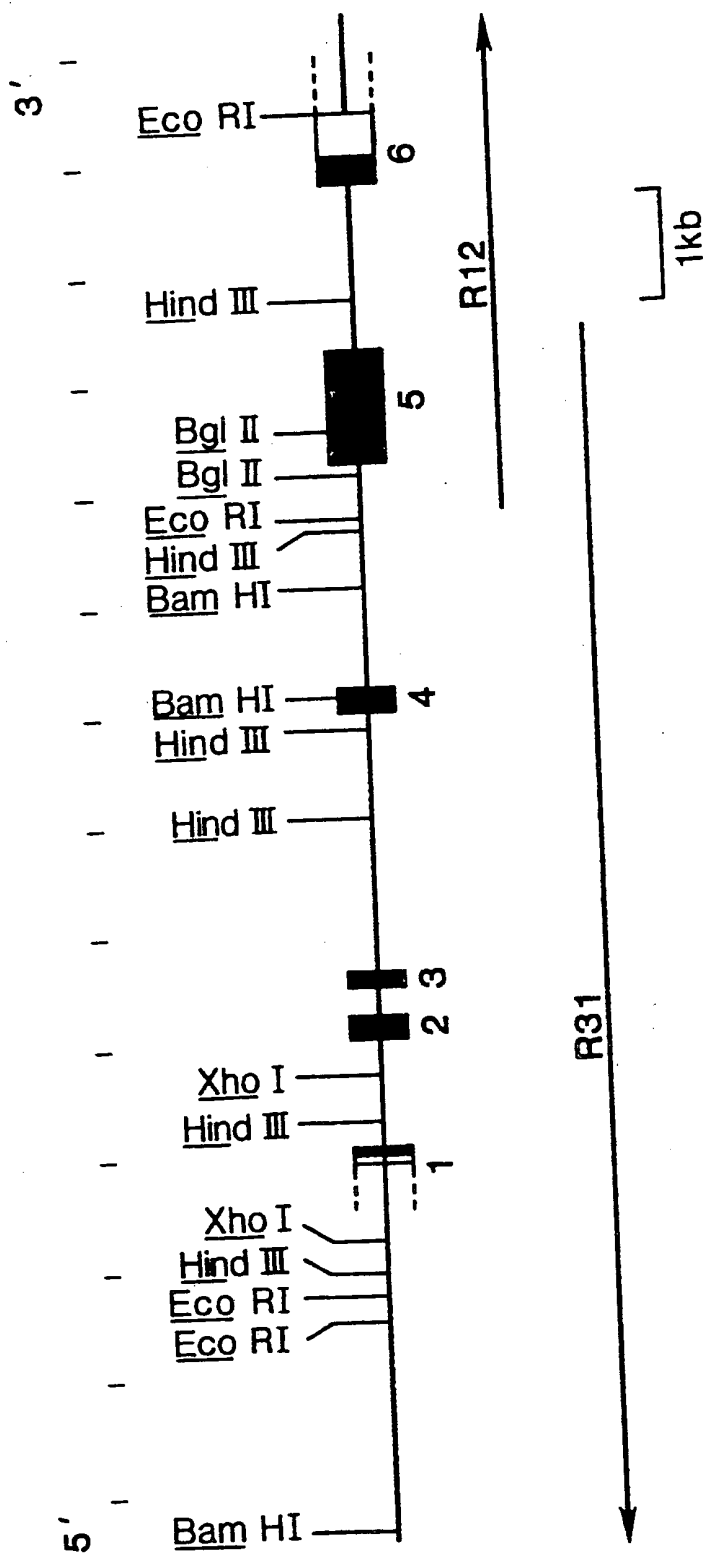


FIG.15A



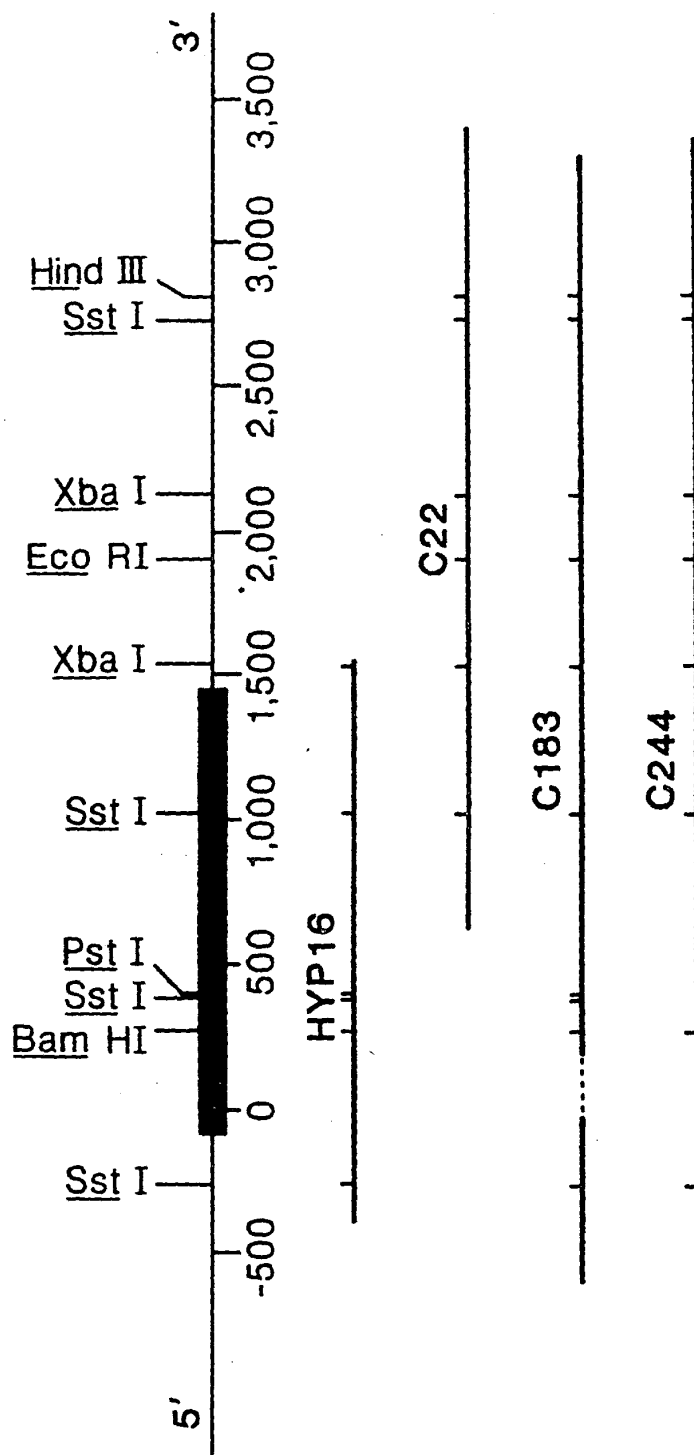


FIG. 15B

5'.....ACTGAGCATTC

-360  
TGTGAACCGAATCACTATCTCCAGGAAGCTAGCCTGAATCCCTCATCCCACAACAGTGCCCTCCCCAACACCTTTGCAGGTTCTGTGTCTGGGCAACCATGAGCTGAAGCAACTGAGCTCTG

-330  
-270

-240  
TTCTGCACCTGTCACTGCTTCCGAGGGACCCCTCGTCAGGCCACCCAGGTTCTCCAGCCGGTTGGTTCTCTGCATCCCTTTGAGGGGCCCTGTCTTCTCTATGACAAATTGCAGAGAGACAGT

-210  
-180  
-150

-120  
GCCTCAAGAAGCCAGCTCTTGGTAGTCCAAGGGMAACCAGGACCCCTCTGAAGCC ATG ACC CTT TCC CAT TCT GCT CTC CAG TTC TGG ACA CAT CTT IAT CTC Met Thr Leu Ser His Ser Ala Leu Gln Phe Trp Thr His Leu Tyr Leu -20

-90  
-60  
-30  
TGG TGT CTC CTT CTG GTG CCA GCA G gtgagt.....tatccccacag TG TTG ACC CAG CAA GGC TCA CAC ACC CAT GCT GAG GAC CGC CTG TTC Trp Cys Leu Leu Val Pro Ala V al Leu Thr Gln Gln Gly Ser His Thr His Ala Glu Asp Arg Leu Phe -10

60  
AAA CAC CTG TTT GGA GGC TAC AAT CGC TGG GCA CGG CCA GTG CCC AAC ACT TCT GAT GTG GTC ATC GTG CGC TTT GGA TTA TCC ATT GCT Lys His Leu Phe Gly Gly Tyr Asn Arg Trp Ala Arg Pro Val Pro Asn 30

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**FIG. 15C-1**



270 ATC TGG ATC CCA GAC ATT GTC CTC TAC AAC AA gtaaga.....ctcttcccag T 330 ACC AAG  
ile Trp ile Pro Asp ile Val Leu Tyr Asn As 100 n Ala Asp Gly Glu Phe Ala Val Thr His 110 Met Thr Lys  
90  
360 GCT CAC CTC TTC TTC ACG GGC Thr Phe Thr Gly 120 420 TTC CCC TTC  
Ala His Leu Phe Phe Phe Thr Gly 130 AGC TCC TGC AGC ATC GAT GTG ACC TTC Phe Pro Phe  
140  
450 GAC CAG CAG AAC TGC AAG ATG AAG 480 ATC GAT CTG GAG CAG ATG GAG AGG ACA 510 GAC CTG  
Asp Gln Gln Asn Cys Lys Met 150 Phe Gly Ser Trp Thr Tyr Asp Lys Ala 160 Lys ile Asp Leu Glu Gln Met Glu Arg Thr Val Asp Leu  
170  
540 AAG GAC TAC TGG GAG AGT GGC GAG 570 TAT AAC AGT AAG AAG TAC GAC TGC TGC GCG GAG ATC TAC  
Lys Asp Tyr Trp Glu Ser Gly 180 Trp Ala ile ile Asn Ala Thr Gly Thr 190 Tyr Asn Ser Lys Lys Tyr Asp Cys Ala 200 Glu ile Tyr  
630 CCC GAT GTC ACC TAC TAC TTT Tyr Phe 210 660 ATC ATC AAC CTC ATC CCA TGC CTG CTC ATC TCC TGC CTC  
Pro Asp Val Thr Tyr Tyr 220 ile Arg Arg Leu Pro Phe Tyr Thr 230 ile Asn Leu ile ile Pro Cys Leu Leu ile 240 Ser Cys Leu  
720 ACT GTG CTC GTG TTC TAC CTG CCT 750 TCC GAG TGT GGA GAG AAG ATC ACG CTG TGC Cys 250 780 TTC CTG CTG  
Thr Val Leu Leu Val Phe Tyr Leu 260 Ser Glu Cys Gly Glu Lys ile Thr Leu 270 Cys 280 Cys 290 Phe Thr Val 300  
810 CTC ATC ACG GAG ATC ATC CCG TCC 840 ACC TCG CTG GTC ATC CCA CTC ATC GGC 870 ACC CTC TCT  
Leu ile Thr Glu ile ile Pro 270 Thr Ser Leu val ile Pro Leu ile Gly 280 Thr Ser Leu Leu Phe Thr Met ile Phe Val 290 Thr Leu Ser

FIG.15C-2

ATC GTT ATC ACA GTC TTC GTG CTC AAT GTA CAC CAC CGC TCC CCC AGC ACC CAC AAC ATG CCC AAC TGG GTA AGG GTA GCC CTG CTA GGC  
Ile Val Ile Thr Val Phe Val Leu Asn Val His His Arg Ser Pro Ser Thr His Asn Met Pro Asn Trp Val Arg Val Ala Ala 960

CGG GTG CCC AGG TGG CTG ATG ATG AAC CGG CCC CTG CCA CCT ATG GAG CTC CAT GGC TCC CCG GAT CTG AAG CTC AGC CCC CTG TCA TAC CAT  
Arg Val Pro Arg Trp Leu Met Met Asn Arg Pro Leu Pro Pro Met Glu Leu His Gly Ser Pro Asp Leu Lys Leu Ser Pro Ser 1050

TGG CTA GAG ACT AAC ATG GAT GCT GGA GAA AGG GAG GAG ACA GAG GAA GAG GAG GAA GAA GAT GAA AAC ATA TGT GTG TGT GCA GGC  
Trp Leu Glu Thr Asn Met Asp Ala Gly Glu Arg Glu Thr Glu Glu Glu Glu Glu Glu Asp Glu Asp Glu Asn Ile Cys Val Cys Ala 1140

CTT CCA GAC TCT TCG ATG GGT GTC CTC TAT GGC CAT GGC GGC CTG CAT CTG AGA GCC ATG GAG CCT GAG ACC AAG ACT CCA TCC CAG GCT  
Leu Pro Asp Ser Ser Met Gly Val Val Leu Tyr Gly His Gly Glu Leu His Leu Arg Ala Met Glu Pro Glu Thr Lys Thr Pro Ser Ser 1230

AGC GAG ATT CTG CTG TCA CCT CAA ATA CAG AAA GCA CTA GAA GGT GTA CAC TAC TAT ATT GCT GAC CGT CTG AGG TCT GAG GAT GCT GAC TCT  
Ser Glu Ile Leu Leu Ser Pro Glu Ile Glu Lys Ala Leu Glu Gly Val His Tyr Ile Ala Asp Arg Leu Arg Ser Glu Asp Ala Ala 1320

TCG gtaagt.....ctaacttcag GTG AAG GAA GAC TGG AAG TAT GTG GCC ATG GTG GTA GAC CGG ATA TTC CTC TGG CTG TTC Phe 1380  
Ser Val Lys Glu Asp Trp Lys Tyr Val Ala Met Val Val Asp Arg Ile Phe Leu Trp Leu Phe Ile 1450

GTC TCG TTC CTG GGG ACC ATC GGA CTC TTC CTT CCT CCA TTC CTG GCT GGA ATG ATC TAA CTTTCATGTCCTTCATGTTGGCTCCCAAGGTGGCCCTTCGTA  
Val Cys Phe Leu Glu Thr Ile Gly Leu Phe Leu Pro Pro Phe Leu Ala Gly Met Ile 1470

1500 ACTATCTCTAGTCTCTGTGAATGGAGCCATCTCTAGAAATACTCTTTTGAC.....3'  
1530

**FIG. 15C-3**

**FIG. 16**



FIG.17A

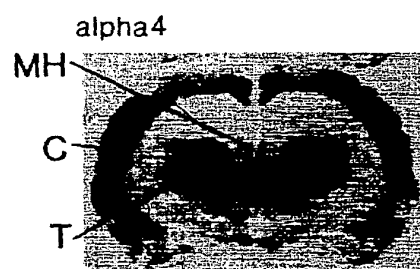
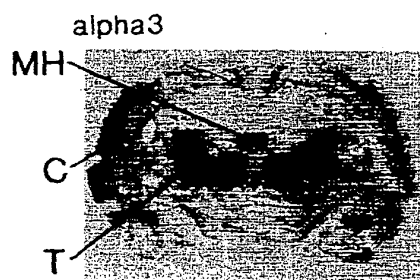
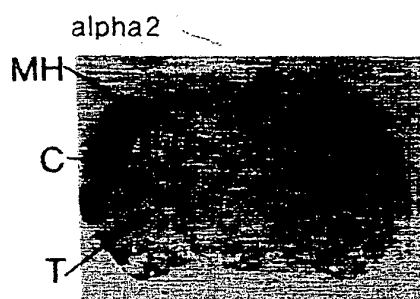
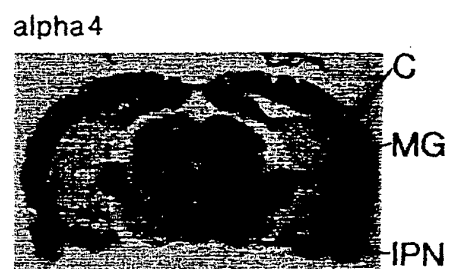
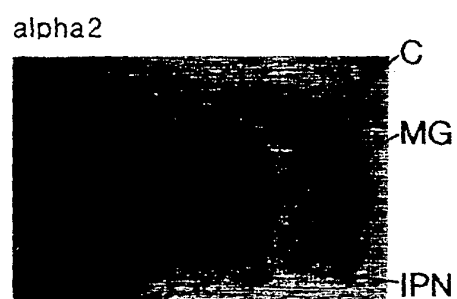


FIG.17B



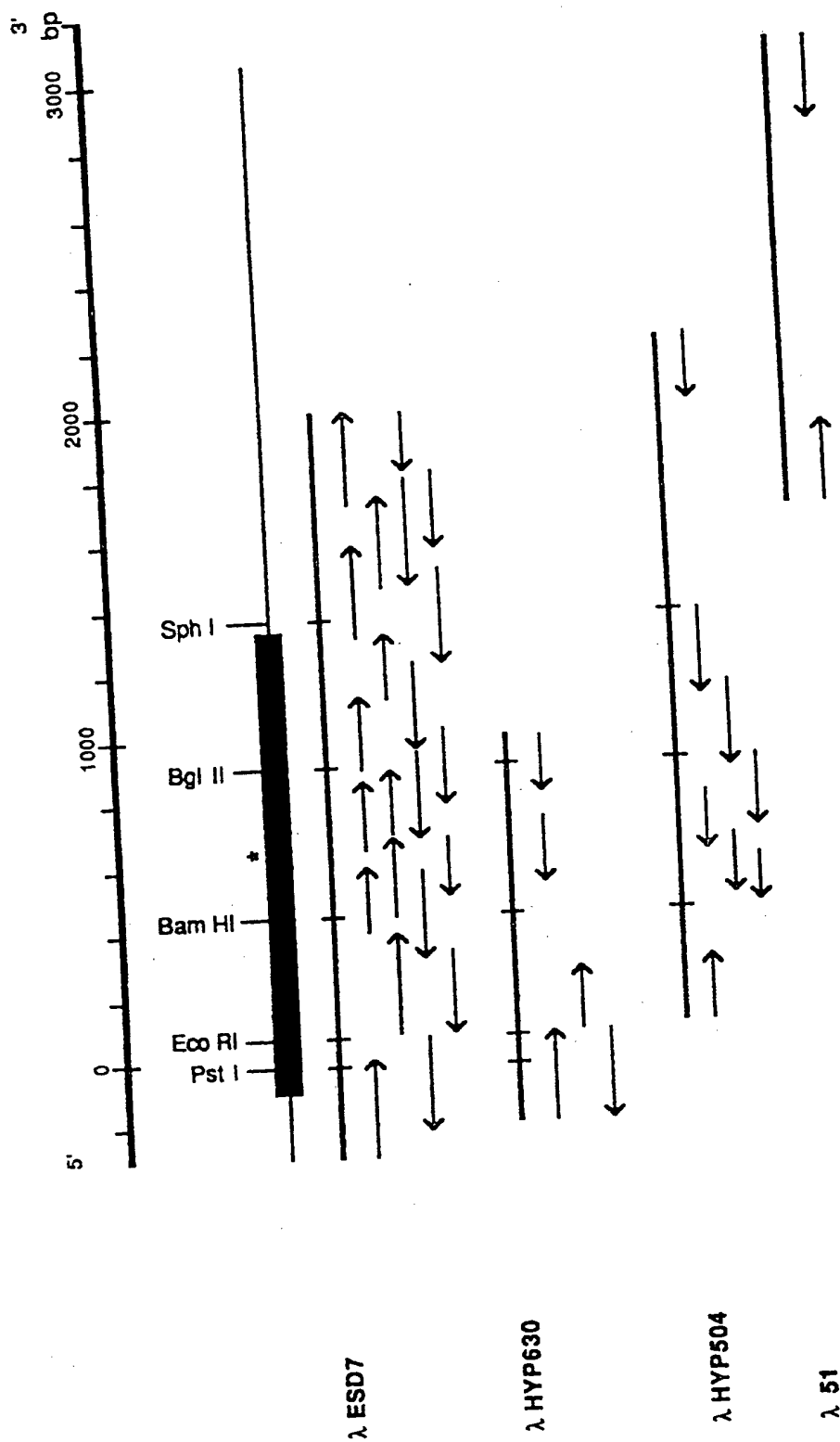


FIG.18A

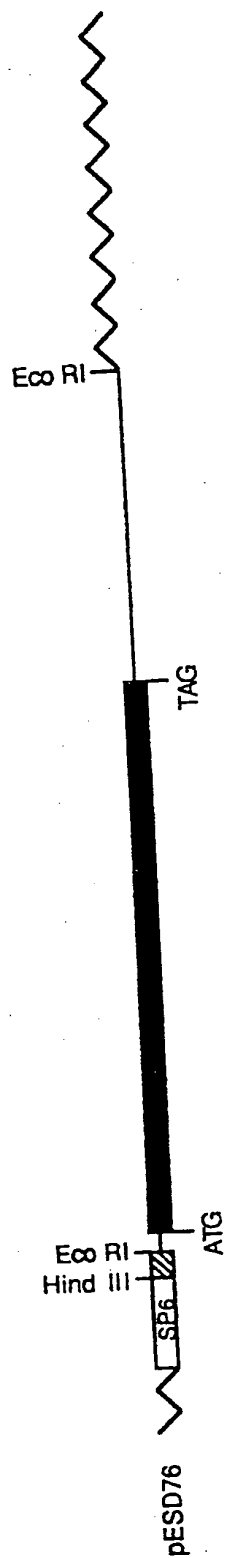


FIG.18B





5' .....GACACACATT  
-240 -220 -200 -180 -160 -140  
TGTGCTCATCAGCTGATTTATTTTCATCAGGCAGCTGGTCCCTGGTTTCATCAGGCTTTGAACCACTACACATTGTTGTTTTTAACCCCTGATCCTTTCCAGTGGAAACACT  
-120 -100 -80 -60 -40  
CTGGGCTTCAAGGAAATGCTCTCTGAAGCAGACGTC ATG ACA GGC TTC CTA AGG GTC TTC TTG GTT CTC AGT GCC ACT CTC TCA GGT TCC TGG GTG  
Met Thr Gly Phe Leu Arg Val Phe Leu Val Leu Ser Ala Thr Leu Ser Gly Ser Trp Val  
-30 -20 -10  
1 10 20 30 40 50 60  
ACT CTT ACG GCC ACT GCA GGA CTC AGC TCA AGC TCA GTC GCT GAA CAC GAA GAC GCA CTC CTC AGA CAT TTG TTC CAA GGT TAC CAG AAA TGG GTC  
-20 -1 1 20 40 60  
Arg Pro Val Leu Asn Ser Ser Asp Ile Ile Lys Val Tyr Phe Gly Leu Lys Ile Ser Gln Leu Val Asp Val Asp Gln Lys Asn Gln Leu  
30 40 50 60 70 80 90 100 110 120 130 140  
CGC CCT GTG TTG AAT TCC AGT GAC ATC ATA AAA GTG TAT TTT GGA TTA AAA ATA TCC CAG CTT GTG GAT GTG GAA AAG AAT CAG CTG  
Met Thr Thr Asn Val Trp TGG CTG AAG CAG GAA TGG ACA GAC CAA AAA TTA CGC TGG AAT CCG GAA GAA TAT GGT GGA ATT AAT TCG ATA AAG  
160 180 200 220 240  
Val Pro Ser Glu Ser Leu Trp Leu Lys Gln Glu Trp Thr Asp Gln Lys Leu Arg Trp Asn Pro Glu Glu Tyr Gly Gly Ile Asn Ser Ile Lys  
60 80 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240  
ATG ACG ACA AAT GTG TGG CTG AAG CAG GAA TGG ACA GAC CAA AAA TTA CGC TGG AAT CCG GAA GAA TAT GGT GGA ATT AAT TCG ATA AAG  
160 180 200 220 240  
Val Pro Ser Glu Ser Leu Trp Leu Lys Gln Glu Trp Thr Asp Gln Lys Leu Arg Trp Asn Pro Glu Glu Tyr Gly Gly Ile Asn Ser Ile Lys  
90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240  
GTT CCA TCA GAA TCG CTC TGG CTG CCG GAC ATA GTT CTC TTT GAA AAT GCT GAC GCA CGT TTT GAG GGC TCC CTC ATG ACC AAG GCC ATT  
260 280 300 320 340 360 380 400 420  
Val Lys Ser Ser Gly Thr Val Ser Trp Thr Pro Pro Ala Ser Tyr Lys Ser Ser Cys Thr Met Asp Val Thr Phe Phe Pro Phe Asp Arg  
120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420  
GTG AAG TCC ACT GGA ACC GTC AGC TGG ACT CCT CCC GCC AGC TAC AAG AGT TCC TGC ACC ATG GAT GTC ACA TTT TTC CCG TTC GAC AGG  
340 360 380 400 420

FIG.19A



150 Gln Asn Cys Ser Met Lys Phe Gly Ser Trp Thr Tyr Asp Gly Thr Met Val Asp Leu Ile Leu Ile Asn Glu Asn Val Asp Arg Lys Asp 170  
CAG AAC TGC TCG ATG AAG TTT GGA TCC TGG ACT TAC GAC GGT ACC ATG GTT GAC CTC ATC CTA ATC GAA AAC GAT GAC CGG AAA GAC 500  
440 460

180 Phe Phe Asp Asn Gly Glu Trp Glu Ile Leu Asn Ala Lys Gly Met Lys Gly Asn Arg Arg Glu Gly Phe Tyr Ser Tyr Pro Phe Val Thr 200  
TTT TTT GAT AAC AAG GGA GAG TGG GAG ATA CTC AAC GCA AAG GGG ATG AAG GGC AAC AGA AGA GAA GGC TTT TAC TCC TAT CCG TTT GTT ACC 600  
520 540 560 580

210 Tyr Ser Phe Val Leu Arg Arg Leu Pro Leu Phe Tyr Thr Leu Phe Leu Ile Ile Pro Cys Leu Gly Leu Ser Phe Leu Thr Val Leu Val 230  
TAC TCT TTT GTC CTG AGA CGC CTG CCC TTG TTT TAC ACC GTC CTC TTT TTG ATA ATC CCC TGC CTG GGG TTG TCT TTT CTC ACG GTC CTG GTG 680  
620 640 \*

240 Phe Tyr Leu Pro Ser Asp Gly Glu Lys Leu Ser Leu Ser Thr Ser Val Leu Val Ser Leu Thr Val Phe Leu Leu Val Ile Glu Glu 260  
TTC TAC CTA CCC TCG GAC GAA GGG GAA AAA CTC TCA TTA TCC ACC TCC GGT TTG GTC TCT TTG ACG GTG TTT CTT TTA GTG ATT GAA GAA 780  
700 720 740 760

270 Ile Ile Pro Ser Ser Lys Val Ile Pro Leu Ile Gly Glu Tyr Leu Leu Phe Ile Met Ile Phe Val Thr Leu Ser Ile Ile Val Thr 290  
ATA ATC CCG TCC TCT TCG AAG GTC ATC CCC CTC ATT GGC GAG TAC CTC CTC TTC ATT ATG ATT TTT GTC ACG CTG TCT ATT ATC GTC ACG 860  
800 820 840

300 Val Phe Val Ile Asn Val His His Arg Ser Ser Ser Thr Tyr His Pro Met Ala Pro Tip Val Lys Arg Leu Phe Leu Gln Arg Leu Pro 320  
GTT TTT GTA ATT ANT GTC CAC CAC CAC AGA TCT TCC TCA ACG TAC CAT CCC ATG GGC CCC TGG GTG AAG AGG CTG TTT CTA CAA AGA CTC CCG 960  
880 900 920 940 960

330 Arg Trp Leu Cys Met Lys Asp Pro Met Asp Arg Phe Ser Phe Pro Asp Gly Lys Glu Ser Asp Thr Ala Val Arg Gly Lys Val Ser Gly 350  
AGA TGG CTT TGC ATG AAG GAC CCC ATG GAC CGC TTC TCT TTC CCG GAT GGA AAG GAG AGT GAT ACA GCC GTG AGG GGG AAA GTC TCA GGC 1040  
980 1000 1020

FIG.19B



Lys Arg Lys Gln Thr Pro Ala Ser Asp Gly Glu Arg Val Leu Val Ala Phe Leu Glu Lys Ala Ser Glu Ser Ile Arg Tyr Ile Ser Arg  
AAA AGG AAA CAG ACT CCC GCC AGC GAT GGA GAA AGA GTT CTG CTC GCT TTC CTC GAG AAG GCC TCC GAG TCC ATC AGA TAC ATT TCG AGG  
1060 1080 1100 1120 1140

His Val Lys Lys Glu His Phe Ile Ser Gln Val Val Gln Asp Trp Lys Phe Val Ala Gln Val Leu Asp Arg Ile Phe Leu Trp Leu Phe  
CAT GTG AAA AAG GAA CAC CAC TTC ATC AGC CAG GTA GTG CAA GAC TGG AAA TTT GTG GCT CAA GTT CTG GAC CGC ATC TTC CTG TGG CTC TTT  
1160 1180 1200 1220 1240

Leu Ile Ala Ser Val Leu Gly Ser Ile Leu Ile Phe Ile Pro Ala Leu Lys Met Trp Ile His Arg Phe His  
CTG ATA GCT TCT GTG TTG GGT TCC ATT CTG ATT TTT ATT CCA GCC TTG AAG ATG TGG ATA CAT CAT CGT TTC CAC TAG GAGCCACTCTCTGACCCCA  
1240 1260 1280 1300 1320

TTTAGAAGACATACATAGACGACATCCACCTTAGGACCTGACAGCGGCTGGCATCTGACAGGAGCAGAGCCATGCAATCGTAGTGGTCCCTGTCTGTGGAGCTTTCTGTG  
1340 1360 1380 1400 1420 1440

ATTGAGGGCAGTACAGAGAAATGTGGTTTGAGTTAGTGTAGTGTGGCTGCCATTAGAGGTGTAGTTGGCAATTTGGAGACGCTCTCCATGTTATATTGTTATGTTGGAGTTCTCTGAAC  
1460 1480 1500 1520 1540 1560

TACTCCCTCTGCTCATCCCTGACGCACTGGGGCTATGTGGTATTCTCTAGCAGTGTGGTGAACGCAATTTTGACAAATAGTTTCAGGAAATTACGAGGTACAACTCTCCACACACAGG  
1580 1600 1620 1640 1660 1680

TCAATTTCGCCACTTGTCAACGAGTGTCCCAAAATAGGGTCATTGAAGATGACCTTGAATGGCTATGACAGTTCTCTAAGGCAGGTGTTTACTGGAAGTTTGTCTCAGCTGACCTGCGAAC  
1700 1720 1740 1760 1780 1800

TTTTCGAATGCAGGTAGGAACTCGGGTGAATTTCTAGCTTGTCTGTAAAGTTCCATCAAAADAACTTACCCAGAAACAGGCCATTCCGCTAGTAGAACTGTATTTATTTCACACATCTC  
1820 1840 1860 1880 1900

TTTTTTTTTCCC.....3'  
1930

FIG.19C



NEURONAL NICOTINIC ACETYLCHOLINE RECEPTOR SUBUNITS

BETA 3 MTGFLRVLVLSATLGGSWTLTATAGLSSVAFEDHALLRHLFGQOKKWRVVLSSDIJKYVFGKISDVLGVQVKKKLLTNVAKLQKQNTDOKLRVWDEEYGGI  
BETA 2 MLACMAGHSNMAFLSFSLWLCGSLGTDTERLVEHLLDPNKLIRATIGSELVTVQVLMVSLACISVHRESITIRVMAIDENEYRRTWKREDFDM  
ALPHA 2 MTLSHSALOFTWLYLWCLLVPAVLTOGSGHTHADRLEFKH LFGGNARWARVPKTSQVIVFFGLSIAIDQOKKARVATIRVAKLQKQNTDOKLRVWDEEYGGI  
ALPHA 3 MGVLVLPPLSMMLVLLPAASASEAERHLEFOY LFEDNEIRIRVANVSHVPIQFEVMSSEIVAKQIVNGLVLLVQVKKKLLTNVAKLQKQNTDOKLRVWDEEYGGI  
ALPHA 4 MEIGGPGAPPPPLLLPLLLGLTGLLPASSHIEIRAHAEERLLKR LFSGAKKWSRVGQISDVVLVRFLGLSIAIDQOKKARVATIRVAKLQKQNTDOKLRVWDEEYGGI  
-----SIGNAL PEPTIDE-----  
BETA 3 NSIKVSESLLPDIVIFENADGRFEGSLMTKIVKSSSTVSTPPASVYKSSCTMDVFFEFQDRNGSWKIGSWTYDGTAVDILINWORKDFDNZEWELNAKG  
BETA 2 KKVRLPSKHIMLPDVLVYNADGAYEVFSYANVSYDGSIFLPPALYKSSCKIEVAFHFPDQDNCQTKFHWITVDRTEIDVLKSDVASLDQTPSSEIWOIIALPG  
ALPHA 2 TSLRVPSSEMIMPDVLVYNADGFAVTHMTKMLFFETVAVWPPALYKSSCKIDVFFEPDQDNCQTKFHWITVDRTEIDVLKSDVASLDQTPSSEIWOIIALPG  
ALPHA 3 EFMRVPAEKIKKPDVLVYNADGFOVDKTKALKLYTSEVTWPPALYKSSCKIDVFFEPDQDNCQTKFHWITVDRTEIDVLKSDVASLDQTPSSEIWOIIALPG  
ALPHA 4 TSIRIDSELIMRDPDVLVYNADGFAVTHMTKMLFFETVAVWPPALYKSSCKIDVFFEPDQDNCQTKFHWITVDRTEIDVLKSDVASLDQTPSSEIWOIIALPG  
BETA 3 MKGNRR EGFYS YPFVTSFVLRRRLFLYILFETIPQGLSFTVVEYLPDQEGEKLSSTVLSVLSIVLLVLEEIPSSKVIITEITELFIMIFVILSVI  
BETA 2 RRNENPDOSTVVDITVDFIIRKRLFYINLITPGVLTITSEALVYLPDQEGEKLSSTVLSVLSIVLLVLEEIPSSKVIITEITELFIMIFVILSVI  
ALPHA 2 TYNSKKYDCCAEI YPDVTVYFVIRRLPLEYINLITPGVLTITSEALVYLPDQEGEKLSSTVLSVLSIVLLVLEEIPSSKVIITEITELFIMIFVILSVI  
ALPHA 3 YKHEIKYNCCAEI YPDITVSLYIRRLPLEYINLITPGVLTITSEALVYLPDQEGEKLSSTVLSVLSIVLLVLEEIPSSKVIITEITELFIMIFVILSVI  
ALPHA 4 TYNTRKYECCEI YPDITVAFIIRRLPLEYINLITPGVLTITSEALVYLPDQEGEKLSSTVLSVLSIVLLVLEEIPSSKVIITEITELFIMIFVILSVI  
-----TMD-----  
BETA 3 TQFVIRVHSSSTVMPAPVKKRLFQRLRRLWLCUKDPMDRFSFPDGK  
BETA 2 SVQVLRVHSSPTITAPVKKVVFLEKLTLLFLDOPRRRCARQLRLRRRQREGEAEVFFREGPAADPCTCFVNP  
ALPHA 2 TQFVLRVHSSPTITAPVKKVVFLEKLTLLFLDOPRRRCARQLRLRRRQREGEAEVFFREGPAADPCTCFVNP  
ALPHA 3 TQFVLRVHSSPTITAPVKKVVFLEKLTLLFLDOPRRRCARQLRLRRRQREGEAEVFFREGPAADPCTCFVNP  
ALPHA 4 TQFVLRVHSSPTITAPVKKVVFLEKLTLLFLDOPRRRCARQLRLRRRQREGEAEVFFREGPAADPCTCFVNP  
-----CYTOPLASMIC REGION-----  
ALPHA 4 PLEVDPDKTSEVEKASPCSPGSCPPPKSSSGAPMLIKARSLVQHVPSQEAEDGIRCSRSLQYCVSDGAASLADSKPTSLKARPSOLPVSDOASPCCKCT  
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BETA 3 ESDTAVRGKVGSRKQTP ASDGERVLVAFLEKASEIRYISRHVKKEHFIQVYVQDQKFAQVDRIFLWLIASVLSILIPALKKWIHRFH  
BETA 2 ASYQGLAGAFRAEPTAAG PGRSVGPGSCGLREAVDGVRFADHMRSEDDQSVRECKWYFAVADRFLWIYFVGVFGTVGMLQPLFONYTATFLHPDHSAPSSK  
ALPHA 2 YHGGLHLRAMEPETKTP SOASEILLSPOIKALEGVHYADRLRESDADSSVKEKMYVAVYERILVLIIVCFGLGTIGLPPFLAGMI  
ALPHA 3 ISNFSANLTRSSSESYN AVLSLSALSPKEIKETOSVKYIAENMKAGINVAKEIQDQWYFAVADRFLWIYFVGVFGTVGMLQPLFONYTATFLHPDHSAPSSK  
ALPHA 4 CKEPSVPSPVTLKAGTKAPPOHPLPLSPALTRVGVGYADHLKAEDTDFSVKEDQWYFAVADRFLWIYFVGVFGTVGMLQPLFONYTATFLHPDHSAPSSK  
-----TMD IV-----

FIG.20

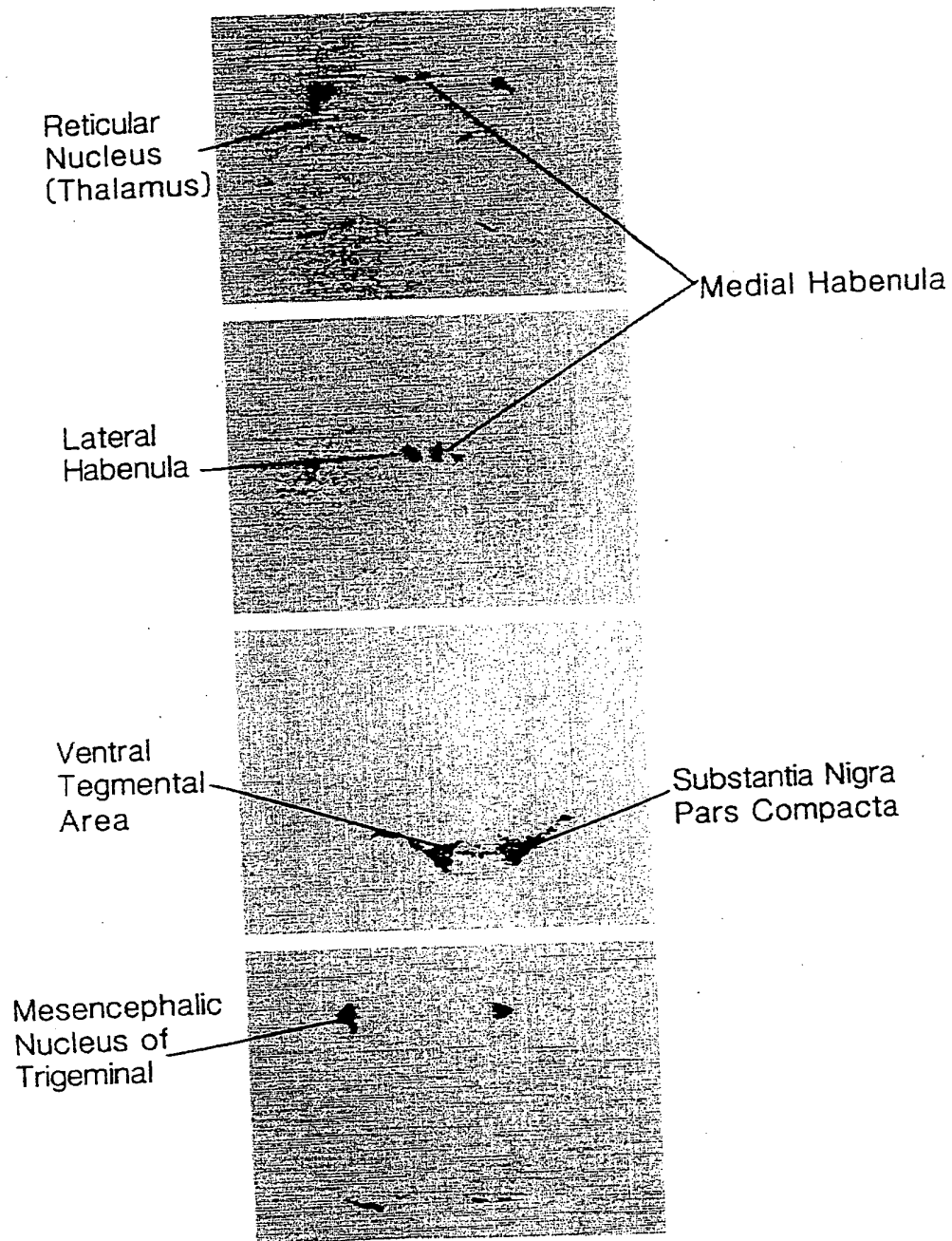
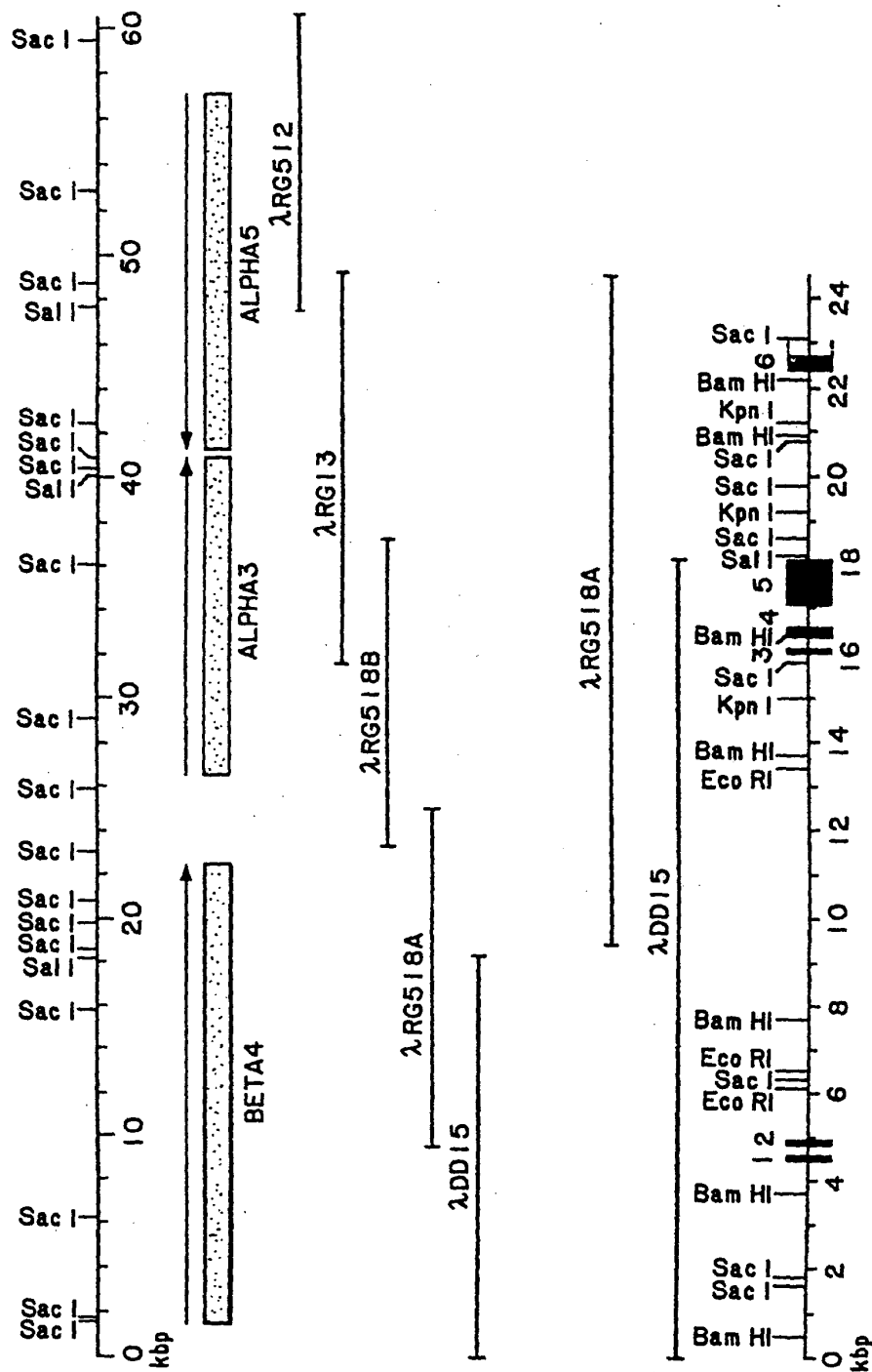


FIG.21



FIG.22

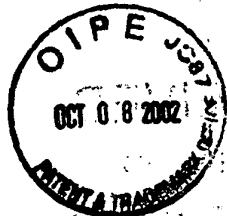




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**FIG. 24A**





130 Ala Ile Tyr Lys Ser Ala Cys Lys Ile Glu Val Lys His Phe Pro Phe Asp Gln Gln Asn Cys Thr Leu Lys Phe Arg Ser Trp Thr Tyr  
GGT ATC TAC AAG AGT GCC TGC AAG ATT GAG GTG AAG CAC CAC TTT CCC TTC GAC CAG CAG AAC TGC ACC CTC AAA TTC CGC TCC TGG ACC TAT  
380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

160 Asp His Thr Glu Ile Asp Met Val Leu Lys Ser Ala Thr Ala Ile Met Asp Phe Thr Pro Ser Gly Glu Trp Asp Ile Val Ala Leu  
GAC CAC ACG GAG ATT GAC ATG GGT CTT AAG TCG CCC ACG GCC ATC ATG GAT GAC TTC ACC CCC AGT GGT GAA TGG GAC ATT GTG GCC CTC  
480 500 520 540 560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

190 Pro Gly Arg Arg Thr Val Asn Pro Gln Asp Pro Ser Tyr Val Asp Val Thr Tyr Asp Phe Ile Ile Lys Arg Lys Pro Leu Phe Tyr Thr  
CCA GGA CGG AGG ACG GTG AAC CCT CAG GAC CCC AGC TAC GTG GAC GTG ACC TAT GAC TTC ATC ATC AAG CGC AAC GCG CTC TTC TAC ACC  
560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

220 Ile Asn Leu Ile Ile Pro Cys Val Leu Ile Thr Ser Leu Ala Ile Leu Val Phe Tyr Leu Pro Ser Asp Cys Gly Glu Lys Met Thr Leu  
ATC AAT CTT ATC ATT CCT TGT GTG CTC ATC ACC TCG CTG GCT ATC CTG GTC TTC TAC CTG CCC TCC GAC TGT GGG GAG AAG ATG ACG CTC  
660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

250 Cys Ile Ser Val Leu Leu Ala Leu Thr Phe Phe Leu Leu Ile Ser Lys Ile Val Pro Pro Thr Ser Leu Asp Ile Pro Leu Ile Gly  
TGC ATC TCT GTG CTG CTG GCA CTC ACG TTC TTC CTC CTG CTC ATC TCC AAG ATC GTC CCT CCC ACC TCC CTC GAC ATA CCG CTC ATT GGC  
740 760 780 800 820 840 860 880 900 920 940 960 980 1000

280 Lys Tyr Leu Leu Phe Thr Met Val Leu Val Thr Phe Ser Ile Val Thr Thr Val Cys Val Leu Asn Val His His Arg Ser Pro Ser Thr  
AAG TAC CTC TTG TTC ACC ATG GTG CTC GTC ACC TTT TCC ATC GTC ACC ACT GTG TGT GTC CTC AAT GTG CAC CAC CGC TCA CCC AGC ACT  
840 860 880 900 920 940 960 980 1000

310 His Thr Met Ala Ser Trp Val Lys Glu Cys Phe Leu His Lys Leu Pro Thr Phe Leu Phe Met Lys Arg Pro Gly Leu Val Ser Leu  
CAC ACC ATG GCA TCC TGG GTC AAG GAG TGC TTC CTC CAC AAA CTG CCC ACC TTC CTC TTC ATG AAG CGT CCC GGT CTT GAA GTC AGC CTC  
920 940 960 980 1000

FIG.24B

340 Val Arg Val Pro His Pro Ser Gln Leu His Leu Ala Thr Ala Asp Thr Ala Ala Thr Ser Ala Leu Gly Pro Thr Ser Pro Ser Asn Leu  
1020 5TC AGG GTC CCT CAT CCC AGC CAG CTG CAC TTT GGC ACC ACA GCT GAT ACT GCA GCC ACC TCT GCC TTA GGC CCC ACC GAT GAT TCC AAC CAC CAC  
1040 350

340 Val Arg Val Pro His Pro Ser Gln Leu His Leu Ala Thr Ala Asp Thr Ala Ala Thr Ser Ala Leu Gly Pro Thr Ser Pro Ser Asn Leu  
1020 5TC AGG GTC CCT CAT CCC AGC CAG CTG CAC TTT GGC ACC ACA GCT GAT ACT GCA GCC ACC TCT GCC TTA GGC CCC ACC GAT GAT TCC AAC CAC CAC  
1040 350

370 Val Asn Pro Val Pro Ala Ala Pro Lys Ser Ala Val Ser Ser His Thr Ala Gln Leu Pro Arg Asp Ala  
1100 TTY GGG AGT TCC ATG TAC TTT GTG AAC CCT GTC CCT GCC GCT CCT AAG TCT GCA GTC AGC TCC CAC ACA GCA GGC CTC CCC AGG GAT GCC  
1120 390

370 Val Asn Pro Val Pro Ala Ala Pro Lys Ser Ala Val Ser Ser His Thr Ala Gln Leu Pro Arg Asp Ala  
1100 TTY GGG AGT TCC ATG TAC TTT GTG AAC CCT GTC CCT GCC GCT CCT AAG TCT GCA GTC AGC TCC CAC ACA GCA GGC CTC CCC AGG GAT GCC  
1120 390

400 Arg Leu Arg Ser Ser Gly Arg Phe Arg Gln Asp Leu Gln Glu Ala Leu Gln Gly Val Ser Phe Ile Ala Gln His Leu Glu Ser Asp Asp  
1200 CGT CTG AGG TCC TCC GGG AGG TTC CGG GAA GAT CTA CAG GAA GCA TTA GAG GGT GTC AGC TTC ATC GCC CAG CAT CTG GAG AGC GAT GAC  
1220 420

400 Arg Leu Arg Ser Ser Gly Arg Phe Arg Gln Asp Leu Gln Glu Ala Leu Gln Gly Val Ser Phe Ile Ala Gln His Leu Glu Ser Asp Asp  
1200 CGT CTG AGG TCC TCC GGG AGG TTC CGG GAA GAT CTA CAG GAA GCA TTA GAG GGT GTC AGC TTC ATC GCC CAG CAT CTG GAG AGC GAT GAC  
1220 420

430 Arg Asp Gln Ser  
1280 CGA GAT CAA AGT gtatgctagt... Val Ile Glu Asp Trp Lys Phe Val Ala Met Val Val Asp Arg Leu Phe Leu Trp  
1300 440

430 Arg Asp Gln Ser  
1280 CGA GAT CAA AGT gtatgctagt... Val Ile Glu Asp Trp Lys Phe Val Ala Met Val Val Asp Arg Leu Phe Leu Trp  
1300 440

450 Val Phe Val Phe Val Cys Ile Leu Gly Thr Met Gly Leu Phe Leu Pro Pro Leu Phe Gln Ile His Ala Pro Ser Lys Asp Ser  
1340 GTG TTC GTG TTT GTG TGT ATT CTG GGC ACC ATG GGG CTC TTC CTC CCA CCC CTT TTC CAG ATC CAC GCA CCC TCC AAC GAC TCC TAG GCT  
1360 470

450 Val Phe Val Phe Val Cys Ile Leu Gly Thr Met Gly Leu Phe Leu Pro Pro Leu Phe Gln Ile His Ala Pro Ser Lys Asp Ser  
1340 GTG TTC GTG TTT GTG TGT ATT CTG GGC ACC ATG GGG CTC TTC CTC CCA CCC CTT TTC CAG ATC CAC GCA CCC TCC AAC GAC TCC TAG GCT  
1360 470

ACCCGGCNTGTCTCGGNNCCGGGAAGCTAGTCAGATGATATGAGAGCGGTGGGAAGCAGGGCGTGTCTTNGGCTACCCGGGCTGTCTCGGCCCCGGGAAGTAGTGAGATGATGATGA  
1420 1440 1460 1480 1500 1520

GAACGGGTGGGAAGCAGCGGGTGTCTTCGG...3'  
1540

**FIG. 24C**

CGTGTCTCGGCCCTCGGGGTCCGGAGATTATCCGCGAGGGCCGCGTCCGCGGGGGGTGCGGGGGTTCGCGGGCGGCGCGCTCGGCTGCTCTTG  
-180 -160 -140 -120 -100

Met Val Gln Leu Leu Ala Gly Arg Trp Arg Pro Thr Gly Ala Arg Arg Gly Thr Ala Gly Gly Leu Pro Gln Leu Ser Ser Ala Lys  
ATG GTG CAG CTG CTG GCA GGG CCG TGG CCG CCG ACC CCG GCG GCG CCG GGC ACG CCG GGC TGG CCT GAA CTA TCC TCT GCT GCT GGC AAA  
-80 -60 -40 -20

His Gln Asp Ser Leu Phe Arg Asp Phe Arg Asp Tyr Gln Arg Trp Val Arg Arg Pro Val Gln His Leu Ser Asp Lys Ile Lys  
CAT GAA GAC AGC TTG TTT AGG GAT TTA TTT GAA GAC TAC TAC GAA AGG TGG GTT CGC CCT GTG GAA CAC CTG AGC GAC AAG ATA AAA ATC AAG  
20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

Phe Gly Leu Ala Ile Ser Gln Leu Val Asp Val Asp Gln Lys Asn Gln Leu Met Thr Thr Asn Val Trp Leu Lys Gln Gln Trp Ile Asp  
TTT GGC CTT GCG ATA GCG ATA TCT CAG TTA GTA GTG GAT GTG GAT GAG GAG AAA AAC CAG CTG ATG ACG ACG AAC GTC TGG TGG CAG GAA TGG ATA GAT  
100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

Val Lys Leu Arg Trp Asn Pro Asp Asp Tyr Gly Gly Ile Lys Ile Arg Val Pro Ser Asp Ser Leu Trp Ile Pro Asp Ile Val Leu  
GTG AAA TTG AGA TGG AAT CCT GAC GAT TAT GGT GGG ATA AAG ATT ATA CGT GTT CCT TCG GAC TCC CTG CTG TGG ATC CCA GAC ATC GTT TTG  
200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

Phe Asp Asn Ala Asp Gly Arg Phe Gln Gly Ala Ser Thr Lys Thr Val Val Arg Tyr Asn Gly Thr Val Thr Trp Thr Gln Pro Ala Asn  
TTT CAG GAT AAT GCA GAT GGA CGT TTT GAA GGG GCC AGC ACG AAA ACA GTT GTC AGG TAC AAC GGC ACT GTC ACG TGG ACG CAA CCA GCA AAC  
280 300 320 340 360 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

Tyr Lys Ser Ser Cys Thr Ile Asp ACC ATC GAC GAT ACC GTT ACC TTT TTC CC6 TTT GAT CTC CAA AAT AAT TGT TCC ATG AAA TTC GGC TCG TGG ACA TAC TAC GAT GGA  
TAC AAA AGT TCT T6C ACC 380 400 420 440 460 480 500 520 540 560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

Ser Gln Val Asp Ile Ile Leu Gln Asp GAC GAC CAA GAT GTC GAC AGA ACA GAC TTT Asp Phe Phe Thr Asp Phe Ile Trp Gln Trp Ile Met Ser Ala Met Gly  
TCC CAG GTT GAT ATA ATC CTA GAG GAG GAC CAG GAT GAT GTC GAC AGA ACA GAC TTT TTT TTC GAC AAT GGA GAG TGG GAA ATC ATG AGC AGC GCG ATG GGG  
460 480 500 520 540 560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

Ser Lys Gly Asn Arg Thr Asp Ser Cys Trp Tyr Trp Tyr Ile Thr Tyr TCC TCC TTT GTG ATT AAG CCG CTG CCT CTC TTC TAT Thr Leu  
AGC AAG GGG AAC CCG AGC GAC ACC GAC Thr Asp Ser Cys Trp Tyr Trp Tyr Ile Thr Tyr TCC TCC TTT GTG ATT AAG CCG CTG CCT CTC TTC TAT Thr Leu  
560 580 600 620 640 660 680 700 720 740 760 780 800 820 840 860 880 900 920 940 960 980 1000

**FIG. 25A**



Phe Leu Ile Ile Pro Cys Ile Gly 220  
TTC CTT ATT ATC CCC TGC ATT 660  
640  
Leu Ser Phe Leu Thr Val Val Val 230  
CTC TCA TTT CTG ACT GTG GTT 680  
680  
Thr Ser Val Leu Val Ser Leu Thr Val Ile Gly 240  
ACC TCA GTG CTC TCT CTG ACT 660  
740  
250  
Val Phe Leu Leu Val Ile Gly 260  
GTC TTC CTT TTT GTG GTA ATC GAA GAG ATC 780  
760  
270  
Tyr Leu Val Phe Thr Met Ile Thr Val Thr Val Phe 280  
TTG GTG TTC ACC CTA TCC ATT ATG GTG ACT GTC 880  
820  
310  
Asn Ala Met Ala Pro Trp Val Arg 320  
AAC GCT ATG GCG CCC TGG GTT CGT AAG ATA 940  
920  
330  
Gln Arg Glu Glu Ala Glu Ser Gly 340  
CAG AGA GAA GAA GCC GAG AGT 1020  
1000  
350  
Val Val Lys Glu Asn Asp Val Arg 360  
GTC GTG AAA GAG AAC GAC GTC CCG GAG 1100  
1100  
370  
Leu Val Ser Ile Ile Gly Thr Leu 380  
CTG GTG TCA ATC ATT GGG ACT 1200  
1180  
240  
Leu Pro Ser Asn Glu Gly Lys Ile Ser Leu Cys  
CTC CCT TCA AAC GAG GGT GAA AAG ATT 720  
700  
260  
Pro Ser Ser Ser Lys Val Ile Pro Leu Ile  
TCA TCT TCC AAA GTC ATA CCC CTG ATT 800  
800  
290  
Phe Ala Ile Asn Ile His Arg Ser Ser Thr His  
TTC TTT GGC ATC AAC ATC CAC CAC CGC TCT TCC 900  
880  
320  
Leu Leu Cys Met Arg Ser His Ala Asp Arg Tyr Phe Thr  
CTG CTC TGC ATG AGA AGT CAT GCG GAT AGG TAC TTC ACT 980  
960  
350  
Gln Ala Ala Leu Asp Cys Ile Arg Tyr Ile Thr Arg His  
GAA GAA GCC GCA CTC GAT TGC ATT CGC TAC ATC ACG AGG CAC 1080  
1060  
380  
Ala Ala Gln Val Leu Asp Arg Met Phe Leu Trp Thr Phe Leu  
ATA TTT GTC CAA GTC CTT GAT CGG ATG TTT TTG TGG ACG TTT CTT 1160  
1140  
410  
Ile Ala Trp Lys Val Ile Val Pro Val His Ile Gly Asn Thr  
TAT AAA TAT TAT TAT ATA GTC CCA GTT CAC ATT GGA AAC ACA 1240  
1220  
1200

FIG.25B



Ile Lys •  
ATT AAG TGA AACCAAGAAATTACCCTGTGGATTAGTGAGCAGTCATGCAGCTCTTAGGACATGTATGCTGTTATGGAATGTGAAGGTAGTTACAATTTGACATAGGCTATAACA  
1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
GATTAGCAATTTCTAACATTGGCTTAATGTTGTCATAGAACTGCAGTAATAAACCCTCAATAGCAACAACACACATTGTCTGCCTGCACTAGTAGAAGGCCCTAGCATCTGCATCCTGGCAA  
1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
ACCCTACCAATTTGCAACCAATGATGAAGGCCATCCTTGGAGTGCTGGAAACTCAACTGTATTTGAAGACTATTAAACTCCCCCAAAATTTAGTAGGAACATATATATGTGTGGTT  
1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
TTGAATTTTCAGAAATGGGCTTTGGGCTTGTAAATTTGCTGGGCTAGCACAAACCTCCTGAGTAGCTGGGACCATGGGTGTGCTCCACTTTGCCCTGTCTGTATTTACAGATATA  
1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
AAATACATCATTTATATAGGAGGTAGGCCATTACTTGGTTTAATAATAACTTAATGTGCTAGTTAGGTTAATTAATATACCTTAATGTGCTAGCTAATGTCTATTGCTGTGAAGAGACATC  
1840 1820 1800 1780 1760 1740 1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
ATGACCATCAACTCTTATAAAGAAACATTTTCATCAGTGTGCTGCTACAGTTTTTGAGGTTTAGCCCAATTATCACAGTGGAAGCATGATAGCATCCAGGTAGACATATAATGCTGGATCC  
1960 1940 1920 1900 1880 1860 1840 1820 1800 1780 1760 1740 1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
AGGAGTTCTCTACATCTGGATCAGCAGGCAGGAGAGAGAGAGAGGCCACTGGACCTGGCTTGAGCATCTGAACCTCAAGCCCCACCTCCAGTGACACACTTCCCCCAACAAGGCC  
2080 2060 2040 2020 2000 1980 1960 1940 1920 1900 1880 1860 1840 1820 1800 1780 1760 1740 1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
ACACCTCCTAATAGTGCCACTTGGTGATCAAGCATTCAGTCTATGGGTCTAGGAGAGCCATTCTCTATTCAAACCCACACTTAATAGGATGCTATTCTTTACTGACATTTTAAATAAG  
2200 2180 2160 2140 2120 2100 2080 2060 2040 2020 2000 1980 1960 1940 1920 1900 1880 1860 1840 1820 1800 1780 1760 1740 1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
CGACAAATGGTAAC TAGAACAATCGTAGGCCACCTTTACTCTTTTATATGGTAATATGGATTGGCTTTTATTAATACTAGTTTTACAGCCCTATCTGAACACATGTAACAGGCAACTCCTG  
2320 2300 2280 2260 2240 2220 2200 2180 2160 2140 2120 2100 2080 2060 2040 2020 2000 1980 1960 1940 1920 1900 1880 1860 1840 1820 1800 1780 1760 1740 1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
CAGACACATTTCTTTGTAATGACTTTATATCCTGCAGTGGCATGTTCTGCTGTAATGACTTTCAGTCTCCTCGTCCACACTCCTCCGGTTAGTAGGCCATTATATGATACATCGCGTATCCCTG  
2440 2420 2400 2380 2360 2340 2320 2300 2280 2260 2240 2220 2200 2180 2160 2140 2120 2100 2080 2060 2040 2020 2000 1980 1960 1940 1920 1900 1880 1860 1840 1820 1800 1780 1760 1740 1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
ATTTCAGAGCAACTGTGCAGTTGCACAGGTTCCACCTCAAAATGGGATGCCATGACTGTGCTGGATAATTCTGTGGAAAAACCACTTCTGAGCTGGATACGGTGCCTCATACCTGTCTCA  
2560 2540 2520 2500 2480 2460 2440 2420 2400 2380 2360 2340 2320 2300 2280 2260 2240 2220 2200 2180 2160 2140 2120 2100 2080 2060 2040 2020 2000 1980 1960 1940 1920 1900 1880 1860 1840 1820 1800 1780 1760 1740 1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
TGCTACTTTTCAGAGGCAGAGGGGAAATTGCTGTGAGTTGTTGGTCAGCCTGGGTTACATATGAGACCCCTGCTCAGAAACCCAAACAAACAACTTCCCCCTGTGAGGTTGATATAAG  
2680 2660 2640 2620 2600 2580 2560 2540 2520 2500 2480 2460 2440 2420 2400 2380 2360 2340 2320 2300 2280 2260 2240 2220 2200 2180 2160 2140 2120 2100 2080 2060 2040 2020 2000 1980 1960 1940 1920 1900 1880 1860 1840 1820 1800 1780 1760 1740 1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20  
CACACTGTATATCCGAATTTGGGGATCCTCTAGAGTCGACCTGCAGGCATGCAAGCTTGGCGTAATCATAGCTGTTTCTGTGTGAATTTGTTATCCG  
2780 2760 2740 2720 2700 2680 2660 2640 2620 2600 2580 2560 2540 2520 2500 2480 2460 2440 2420 2400 2380 2360 2340 2320 2300 2280 2260 2240 2220 2200 2180 2160 2140 2120 2100 2080 2060 2040 2020 2000 1980 1960 1940 1920 1900 1880 1860 1840 1820 1800 1780 1760 1740 1720 1700 1680 1660 1640 1620 1600 1580 1560 1540 1520 1500 1480 1460 1440 1420 1400 1380 1360 1340 1320 1300 1280 1260 1240 1220 1200 1180 1160 1140 1120 1100 1080 1060 1040 1020 1000 980 960 940 920 900 880 860 840 820 800 780 760 740 720 700 680 660 640 620 600 580 560 540 520 500 480 460 440 420 400 380 360 340 320 300 280 260 240 220 200 180 160 140 120 100 80 60 40 20

FIG.25C



BETA2 MLCMHGSHNSHALFSILLWLCGVLGTDTEERLVEHLDDPSRYNKLIRPATNGSELVTVOLMVSLAQLISVHEREQIMTTNVLTQEWEDYRLTWKPEDFDHMK  
BETA3 MTGFLRVFLVLSATLSGSWVLTATAGLSSVAEHEDALLRHLFGQYQKWPVPLNSDIIKIVYFGLKISQLVDVDEKNQIMTTNVWLKQEWTDQKLWNPEEYGGIN  
BETA4 MRGTPLLVLSLFLQDQDCRLANAEKIMDDLLNKNRYNNLIRPATSSQLISIRLELSQLISVNEREQIMTTISWLKQEWTDYRLAWNSSCYEGVN  
----- SIGNAL PEPTIDE -----

BETA2 KVRLPKXHWLPDVVLYNNADGMYEVSFYSHNAVSYDGSIFWLPPIAYKSAKIEVKHFFPQQNCTMKFRSWTYDRTEIDLVLKSDVASLODFTTPSGENDIIALPG  
BETA3 SIKVPSSEWLPLDIVLFENADGRFEGSLMTRKAIKVSCTVSWTPASYSKSSCTMDVTFPPDRQNCMKFGSWTYDGTMDVLILINENVDRKOFDNGEWEILNARG  
BETA4 ILRIPAKRVWLPDIVLYNNADGMYEVSFYSHNAVSYDGSIFWLPPIAYKSAKIEVKHFFPQQNCTMKFRSWTYDRTEIDLVLKSDVASLODFTTPSGENDIIALPG

BETA2 RRNENPDOS TYVDITYDFIIRKPLFYTTINLIIPCVLITSLAILVFLPSPDCGERMTLCISVLLALTVELLLIGKIVPPTSLDVLVGVKYLMTMVLVTSIVTSV  
BETA3 MKGHNREGYSYFVTYSFVLRRLPLFYTTLELIIPCGLSFLTVLVFLYLPSPDEGEKLSLTSVLVSLTVLVLVIEELIPSSKNVPLIGEXLLFMIFVLSIIVTV  
BETA4 RRTVNPQDP SYVDVITYDFIIRKPLFYTTINLIIPCVLITSLAILVFLPSPDCGERMTLCISVLLALTVELLLIGKIVPPTSLDVLVGVKYLMTMVLVTSIVTSV  
----- MSR I ----- MSR II ----- MSR III -----

BETA2 CVLNVHHRSPST HTMAPWVKVVFLEKLPITLFLQPPHRCARQRLRRRQREGEAVFFREGPAADPCSVGPCSCG  
BETA3 FVINVHHRSSSTYHEMAPWVKRLFLQRLPRWLCMKDPNDRFSFPDGKESDTAVRGVSKRKQTPASDGERVLVAFLEK  
BETA4 CVLNVHHRSPST HTMASWVKECFLHKLPITLFLNKRPGLEVSLVRPHPSQLHLATADTAATSAIGPTSFNSLYGSSMYFVNPVPAAPKSAVSSHAGLPRDARLRS  
----- MSR IV -----

BETA2 LREAVDGVRFIADHMRSEDDDDQSVREDWKYVAMVIDRLFLWIFVFCVGVGMFLQPLFONVYATTFLHPDHSAPSSK\*  
BETA3 ASESIYISRHVKKEHFISQVVDWKFVAQVLDRLFLWFLIASVLGSLILIFIPALKMNIHRFH\*  
BETA4 SGRFREDLQEALEGVSFIAQHLESDDRDQSVIEDWKYVAMVVDRLFLWIFVFCVGVGMFLQPLFONVYATTFLHPDHSAPSSK\*

FIG.26



ALPHA2 MTLSHSALQFWTHLYMCLLLVPAVLTOQGSHTHAEDRLFXHLFGGYNRWARPVPNTSDUVIVRFGLSIAQLIDVDENQOMMTTNVWLKQEWNDYKLRNDPAE  
ALPHA3 MGVLPLPPLSMLMLVLMPLPAASASEAHERLFQYLFEDYNEIIRPVANVSHPVIIQFEVSMQSVKVDENVQIMETNMLKQWMDYKLRNDPSPD  
ALPHA4 MEIGGPGAPPPILLPLLLLTGLTGLLPASSHETRAHAEEELLKRLFGYNGKMSRPVGNISDVULVRFGLSIAQLIDVDENQOMMTTNVWLKQEWNDYKLRNDPSPD  
ALPHA5 MVQLLAGRWRTGARRGTAGGLPELSSAAKHEDSLFRDLFEDYERWVRVEHLSDKIKIFGLAISQLVDVDENQOMMTTNVWLKQEWNDYKLRNDPDD  
SIGNAL PEPTIDE

ALPHA2 FGNVTSRVPSEMIWIPDIVLNNADGEFAVTHMTRAHLFTGTVHVWPPAIYKSSCIDVTFPPDQONCKMKFGSWTYDKAKIDLQOMERTVDLKDYMESGEWA  
ALPHA3 YQGVFHRVPAEKIMKPDIVLYNNADGDFQVDDKTRALLKYTGVTWIPPAIFKSSCKIDVTFPPDQONCKMKFGSWTYDKAKIDLQOMERTVDLKDYMESGEWA  
ALPHA4 YENVTSIRIPSELIWIPDIVLNNADGDFAVTHLTKARLFYDGRVQWTPAIYKSSCIDVTFPPDQONCKMKFGSWTYDKAKIDLQOMERTVDLKDYMESGEWA  
ALPHA5 YGGIKIIRVPSDSLWIPDIVLNNADGREGAS TKTVRYNGTGTWTPANYKSSCTIDVTFPPDQONCKMKFGSWTYDKAKIDLQOMERTVDLKDYMESGEWA

ALPHA2 IINATGYNSKKYDCCAEIYPOVTYYFVIRBLPLFYINLIIPCLLISCLTVLVFYLPSECGEKITLCISVLLSLTVFLLLTIEIIPSTSLVPLIGEYLLFTMIF  
ALPHA3 IIRKAGYKHEIKYNCCEIYQDITYSLYIRRLPLFYINLIIPCLLISCLTVLVFYLPSECGEKITLCISVLLSLTVFLLLTIEIIPSTSLVPLIGEYLLFTMIF  
ALPHA4 IVDVAGYNTKRYKCEAEIYPDITYAFIIRRLPLFYINLIIPCLLISCLTVLVFYLPSECGEKITLCISVLLSLTVFLLLTIEIIPSTSLVPLIGEYLLFTMIF  
ALPHA5 INSAMGSKGNRTDSCCM YPIITYSFVIRBLPLFYINLIIPCLLISCLTVLVFYLPSECGEKITLCISVLLSLTVFLLLTIEIIPSTSLVPLIGEYLLFTMIF  
MSR I MSR II MSR III

ALPHA2 VTLSIVITVFLNVHHRSPSTHNMN MVRVALLGRVPRWLMNMRPLPPMELHSGPOLKLPSPYHMLETNMDAGERETEEREEEDENICVCAGLPDSSMGVLYG  
ALPHA3 VTLSIVITVFLNVHHRSPSTHNMN MVRVALLGRVPRWLMNMRPLPPMELHSGPOLKLPSPYHMLETNMDAGERETEEREEEDENICVCAGLPDSSMGVLYG  
ALPHA4 VTLSIVITVFLNVHHRSPSTHNMN MVRVALLGRVPRWLMNMRPLPPMELHSGPOLKLPSPYHMLETNMDAGERETEEREEEDENICVCAGLPDSSMGVLYG  
ALPHA5 VTLSIVITVFLNVHHRSPSTHNMN MVRVALLGRVPRWLMNMRPLPPMELHSGPOLKLPSPYHMLETNMDAGERETEEREEEDENICVCAGLPDSSMGVLYG

ALPHA2 HGGLHLRAMEPETKTPSQA  
ALPHA3 TRSSSSSESVNAV  
ALPHA4 TCRSPPLEVPDLXTSEVENKASPCSPGSPGPPKSSSGAPMLIKARSLSVQHVPSSQEAEDGIRCRSRISQYCVSQDGAASLADSNKPTSPSTSLKARPSQLPVSDQ  
ALPHA5

ALPHA2 SKILLSPOIKALEGVHYIADIRSEDADSSVKEDWKYVAMVVDRIFLWLFIIIVCFLGTIGLFPPLAGMI\*  
ALPHA3 SLSALSPEIKAEIOSVKYIAENKKAONVAKEIQDDWKYVAMVIDRIFLWVFIIVCFLGTAGLFLQPLMARDDT\*  
ALPHA4 ASPCKCTCKEPPSPVTVLKAGGTAKPPQHLPLSPALTRAVEGVQYIADHLKAEDTFSVKEDWKYVAMVIDRIFLWVFIIVCFLGTAGLFLQPLMARDDT\*  
ALPHA5 LEAALDCIRYITRHHVVKENDREVEDWKFIQAQVLDRMFLWTFLLVSIIGTLGLFVPVFIINGPI\*  
MSR IV

FIG.27

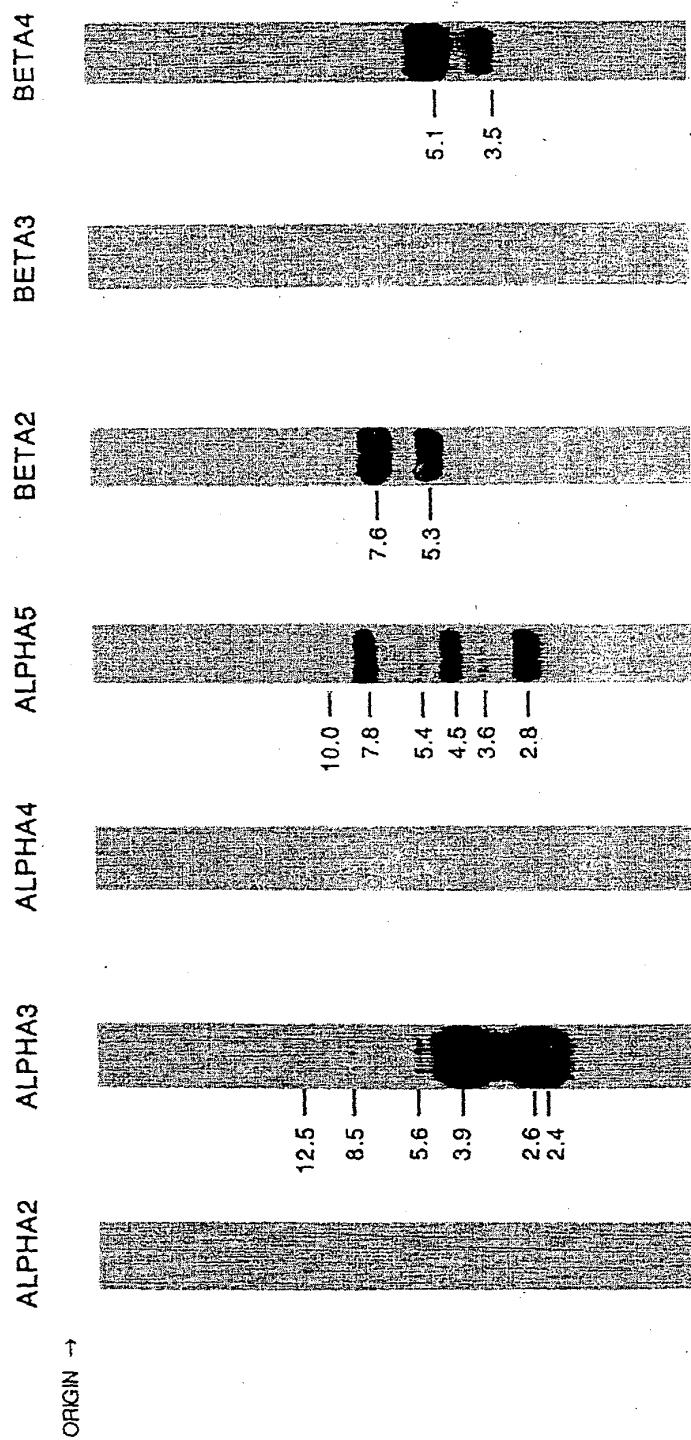


FIG.28



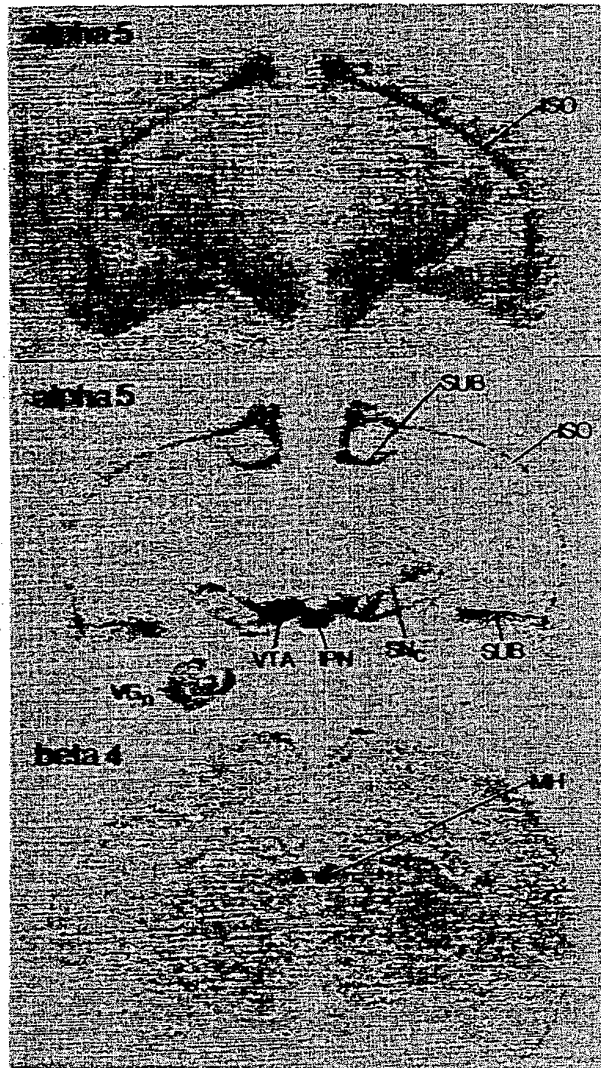


FIG.29